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STUDY OF RELATIONSHIP BETWEEN PLASMA HOMOCYSTEINE LEVELS AND GESTATIONAL HYPERTENSION

A DISSERTATION SUBMITTED TO THE
TAMILNADU Dr M.G.R. MEDICAL UNIVERSITY

IN PARTIAL FULFILLMENT OF THE REGULATIONS FOR THE AWARD OF DEGREE OF

M.D (BRANCH II) OBSTETRICS AND GYNAECOLOGY

COIMBATORE MEDICAL COLLEGE
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CERTIFICATE

This is to certify that this dissertation entitled **"STUDY OF RELATIONSHIP BETWEEN PLASMA HOMOCYSTEINE LEVELS AND GESTATIONAL HYPERTENSION"** is a bonafide work done by **Dr.NIVEDHITHA AARTHY.G** under my guidance and supervision in the department of Obstetrics and Gynaecology during the period of her post graduate study at Coimbatore Medical College, Coimbatore for the Degree of M.D. Obstetrics and Gynaecology from 2009-2012.

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The Ethics Committee, Coimbatore Medical College has decided to inform that your Dissertation is accepted / ~~Not accepted~~ and you are permitted / ~~Not Permitted~~ to proceed with the above Study.

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DECLARATION

I hereby solemnly declare that the dissertation titled "**STUDY OF RELATIONSHIP BETWEEN PLASMA HOMOCYSTEINE LEVELS AND GESTATIONAL HYPERTENSION"** has been prepared by me.

This is submitted to **THE TAMILNADU Dr M.G.R. MEDICAL UNIVERSITY, CHENNAI** in partial fulfillment of the requirements for the award of M.D., Degree examination (Obstetrics and Gynaecology) to be held in April 2012.

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Dr. NIVEDHITHA AARTHY.G

CONTENTS

STUDY OF RELATIONSHIP BETWEEN PLASMA HOMOCYSTEINE LEVELS AND GESTATIONAL HYPERTENSION

KEYWORDS: Homocysteine, Hypertension, Pregnancy.

ABSTRACT:

OBJECTIVE:

To find out the relationship between plasma homocysteine levels and occurrence of gestational hypertension.

METHODS:

A case control study with 50 cases who were postnatal patients with gestational hypertension and 61 controls who were postnatal patients with uncomplicated obstetric histories. Of the 50 cases, 16 had gestational hypertension, 26 had preeclampsia and 8 had Eclampsia. Plasma homocysteine was determined by Chemi luminescence immunoassay method. For statistical analysis chi square test and the student t test were used. Pearson co-relation coefficient was used to detect the correlation.

RESULTS:

Mean Plasma homocysteine levels were found to be significantly higher in cases compared to controls. Mean Plasma homocysteine levels in normal mothers was 10.50µmol/L, in mothers with gestational hypertension was 16.43µmol/L and in preeclampsia was 20.23µmol/L. There was significant association between positive family history of cardiovascular disease and gestational hypertension ($p<0.001$). There was also significant association between plasma homocysteine and positive family history of cardiovascular disease ($p<0.05$). Significant association existed between plasma homocysteine levels and gestational hypertension ($p<0.001$). Plasma homocysteine levels in preeclampsia are higher than that in gestational hypertension ($p<0.001$). Positive correlation was found between plasma homocysteine levels and Mean Arterial Pressure ($r=0.447$, $p=0.000$), Systolic Blood Pressure ($r=0.559$, $p=0.000$) and Diastolic Blood Pressure ($r=0.334$, $p=0.000$).

CONCLUSION:

A relationship exists between plasma homocysteine levels and gestational hypertension. Higher levels of plasma homocysteine levels are found in women with gestational hypertension compared to normotensive pregnant women.

INTRODUCTION

Hypertensive disorders represent the most common medical complication of pregnancy with a reported incidence between 5 and 10 percent. The term hypertension in pregnancy is commonly used to describe a wide spectrum of patients who may have only mild elevations in blood pressure or severe hypertension with various organ dysfunctions.

The three most common forms of hypertension are gestational hypertension, preeclampsia and chronic essential hypertension.

Hypertensive disorders together with haemorrhage and infection form a deadly triad that contribute greatly to maternal morbidity and mortality. In India it accounts for 24% of all maternal deaths. Among the three leading causes of the maternal death, Hypertensive disorders top the list. It is also a major cause of preterm birth, intrauterine growth restriction and perinatal mortality.

How pregnancy incites or aggravates hypertension remains unsolved despite, decades of intensive research. Indeed hypertensive disorders remain among the most significant and intriguing unsolved

problems in Obstetrics. The risk factors are still not well understood, so there is lack of sensitive tests.

Recent research also reveals that many changes precede any increase in BP and though the symptoms and signs usually become apparent in the third trimester, the underlying pathophysiological mechanisms appear between 8-18 weeks of gestation.

Endothelial damage has been implicated in the etiology of gestational hypertension. Homocysteine is a non protein sulphur containing aminoacid which is notorious for causing endothelial damage. It has been proved that homocysteine has a definite role in the setting of coronary artery disease, peripheral arterial disease, Cerebrovascular disease, DVT and Neural tube defects.

The incidence of gestational hypertension is high about 15% to 18% in Coimbatore. The reason could be its unique climate because of the flow of cool breeze all round the year through the Palakkad gap of Western Ghats. Further there are other possible factors such as concentration of industrial labour force due to the presence of more textile and engineering industries, conglomeration of different ethnic populous and the geographical location, which could be the other reasons. The etiology is yet to be unraveled.

Hence studies on gestational hypertension are the need of the hour. With this background this study aims at finding the relationship between plasma homocysteine and gestational hypertension.

Aims and Objectives

AIMS AND OBJECTIVES

Aims:

This study is designed to find out the relationship between plasma homocysteine levels and occurrence of gestational hypertension.

Objectives:

- To measure plasma homocysteine levels in normotensive and gestational hypertension patients.
- To compare plasma homocysteine levels in both the groups.
- To establish a relationship between plasma homocysteine and gestational hypertension.
- To find out possible factors that might influence plasma homocysteine levels in hypertensive disorders of pregnancy.

Review of Literature

REVIEW OF LITERATURE

GESTATIONAL HYPERTENSION

HISTORICAL PERSPECTIVE

Gestational hypertension contributes to the ancient times. Eclampsia was identified by the pre Hippocratic Kahun papyrus from Egypt 3000 years back. PIH was recognized by ancient Greeks. They believed that in pregnant women, the appearance of heaviness, drowsiness and headaches is not a good sign and that they have the possibility to develop some kinds of seizures.

Galen's commentary on Hippocrates aphorisms recommends that he was familiar with the aggressive features in pregnant women[1, 2].

St.Gall, a well known practitioner in the 10 th century AD had a trick played on him. He was about to examine the Duke of Bavaria and as a deception the valuable nobleman replaced for his urine that of a woman who was pregnant. After examination St. Gall made a statement that the Duke would give birth to a child. This event is possibly the first evidence of finding protein in urine of pregnant woman.

Technical description on PIH actually started indirectly in 17th century. The term eclampsia appeared in a treatise on Gynaecology written by Varandaeus in 1619. It was coined by Hippocrates, meaning flash[1, 35, 42].

Blundell, Mauriceau and Bartonand, all these three have documented the signs of PIH. In the year 1840, Rayer detected protein in urine of three pregnant women with edema who had PIH. Old time practitioners of medicine though crude by today's standard, had documented raised blood pressure in women with PIH by examining their stiff bounding pulses.

In 1884, Vinay used ancient sphygmomanometer to measure BP. Further research was conducted in the ensuing years and now it is at the current scenario.

If we look at the past, present and think of future with reference to the relevancy of this disease, it is evident that the names have been ever changing from toxaemia to gestosis and so on, but the disease continues unabated with high materno-fetal loss, however the research also continues [2,38] unabatedly without any pause.

TERMINOLOGY & CLASSIFICATION

The term gestational hypertension was chosen by Dr. Jack Pritchard to describe any new onset uncomplicated hypertension during pregnancy when no evidence of the preeclampsia syndrome was apparent.

The working group classification of hypertensive disorders complicating pregnancy describes four types of hypertensive disease[3]:

1. Gestational Hypertension- Formerly termed pregnancy induced Hypertension. If preeclampsia syndrome does not develop and hypertension resolves by 12 weeks postpartum, it is redesignated as transient hypertension.
2. Preeclampsia & eclampsia syndrome
3. Preeclampsia syndrome superimposed on chronic hypertension
4. Chronic hypertension

An important feature of this classification is differentiating preeclampsia & eclampsia from other hypertensive disorders because former two are potentially more ominous.

Gestational Hypertension:

- Systolic BP>140 or diastolic BP> 90mm Hg for first time during pregnancy.

- No proteinuria
- BP returns to normal before 12 weeks postpartum
- Final diagnosis made only postpartum
- May have other signs & symptoms of preeclampsia. For example epigastric discomfort, thrombocytopenia [3,6,11].

Preeclampsia

Minimum criteria

- BP>140/90mmHg after 20 weeks gestation, proteinuria > 300mg/24hours or > 1+ dipstick.

Increased certainty of preeclampsia:

- BP > 160/110mmHg
- Proteinuria 2.0g/24hours or > 2+ dipstick
- Serum creatinine >1.2mg/dl unless known to be previously elevated
- Platelets <1,00,000/µl
- Microangiopathic hemolysis – increased LDH
- Elevated serum transaminase levels-ALT\AST
- Persistent headache or other cerebral or visual disturbance.
- Persistent epigastric pain

- Preeclampsia is best described as a pregnancy specific syndrome that can affect virtually every organ system.
- Some women may have a typical preeclampsia with all aspects of syndrome but without hypertension or proteinuria or both[11,12,14].
- Indicators of severity of Gestational Hypertensive disorders.

Abnormality	Non severe	Severe
Diastolic BP	<110mm Hg	>110mm Hg
Systolic BP	<160mm Hg	>160mm Hg
Proteinuria	<2+	>3+
Headache	Absent	Present
Visual disturbances	Absent	Present
Upper Abdominal Pain	Absent	Present
Oliguria	Absent	Present
Convulsion	Absent	Present
Serum creatinine	Normal	Elevated

Thrombocytopenia	Absent	Present
Serum Transaminase elevation	Minimal	Marked
Fetal growth restriction	Absent	Obvious
Pulmonary Edema	Absent	Present

The differentiation between non severe & severe gestational hypertension or preeclampsia can be misleading because what might be apparently mild disease may progress rapidly to severe disease.

ECLAMPSIA

- Seizures that cannot be attributed to other causes in a woman with preeclampsia.

SUPERIMPOSED PREECLAMPSIA ON CHRONIC HYPERTENSION:

- New onset proteinuria >300mg/24hours in hypertensive women but no proteinuria before 20 weeks gestation.
- A sudden increase in proteinuria or blood pressure or platelet count <1,00,000/µl in woman with hypertension & proteinuria before 20 weeks gestation.

CHRONIC HYPERTENSION

- BP>140/90mm Hg before pregnancy or diagnosed before 20 weeks gestation not attributable to gestational trophoblastic disease.

(or)

- Hypertension first diagnosed after 20 weeks gestation & persistent after 12 weeks postpartum[34,35,39].

RISK FACTORS FOR HYPERTENSIVE DISORDERS IN PREGNANCY[20,21]:

Genetic Factors:

- Genetic pre-disposition
- Race & ethnicity- more common in Blacks & Asians
- Family History of preeclampsia
- Pregnancy by ovum donation

Age and parity:

- Teenage pregnancy
- Age more than 40 years
- Long interval between pregnancies
- Nulliparity

Partner related factors:

- Change of partner
- Partner who fathered a pre-eclamptic pregnancy in another woman
- Limited sperm exposure

- ❖ Pregnancy due to donor insemination

Presence of underlying disorder:

- ❖ Chronic hypertension
- ❖ Diabetes mellitus
- ❖ Renal disease
- ❖ Obesity (body mass index > 35kg/m^2)
- ❖ Maternal low birth weight
- ❖ Polycystic ovarian syndrome
- ❖ Migraine
- ❖ Collagen vascular disorders
- ❖ Uncontrolled hyperthyroidism
- ❖ Factor V Leiden deficiency
- ❖ Activated protein C deficiency
- ❖ Thrombophilia
- ❖ Sickle cell disease & other hemoglobinopathies
- ❖ Antiphospholipid antibodies
- ❖ **HYPERHOMOCYSTEINEMIA**
- ❖ Protein S deficiency
- ❖ Women with excessive snoring
- ❖ Previous preterm birth

Pregnancy related risk factor:

- Multiple pregnancies
- Hydatidiform mole
- Hydrops fetalis
- Congenital & chromosomal fetal anomalies (Trisomy 13 and Triploidy)
- Urinary tract infection

Miscellaneous factors

- Smoking (reduced risk)
- Psychological strain & stress at work place
- Previous history of preeclampsia
- Raised blood pressure (diastolic >80mm Hg) at booking[38,39,45].

PATHOGENESIS

Hypertensive disorder of pregnancy continues to be a disease of theories & no one theory can explain its etiopathogenesis probably more than one theory works. As Boyd stated it remains

"die krankheit der theorien "

– The disease of theories.

Any satisfactory theory must account for the observation that gestational hypertensive disorders are more likely to develop in women who

- ❖ Are exposed to chorionic villi for the first time
- ❖ Are exposed to super abundance of chorionic villi
- ❖ Have preexisting renal or cardio vascular disease
- ❖ Are genetically predisposed to hypertension developing during pregnancy

A fetus is not a requisite for preeclampsia. Although chorionic villi are essential, they need not be located within the uterus. The

cascade of events that lead to preeclampsia syndrome are characterized by a host of abnormalities that result in endothelial damage, vasospasm, transudation of plasma, ischemic & thrombotic sequeale[4,5].

INFLAMMATION

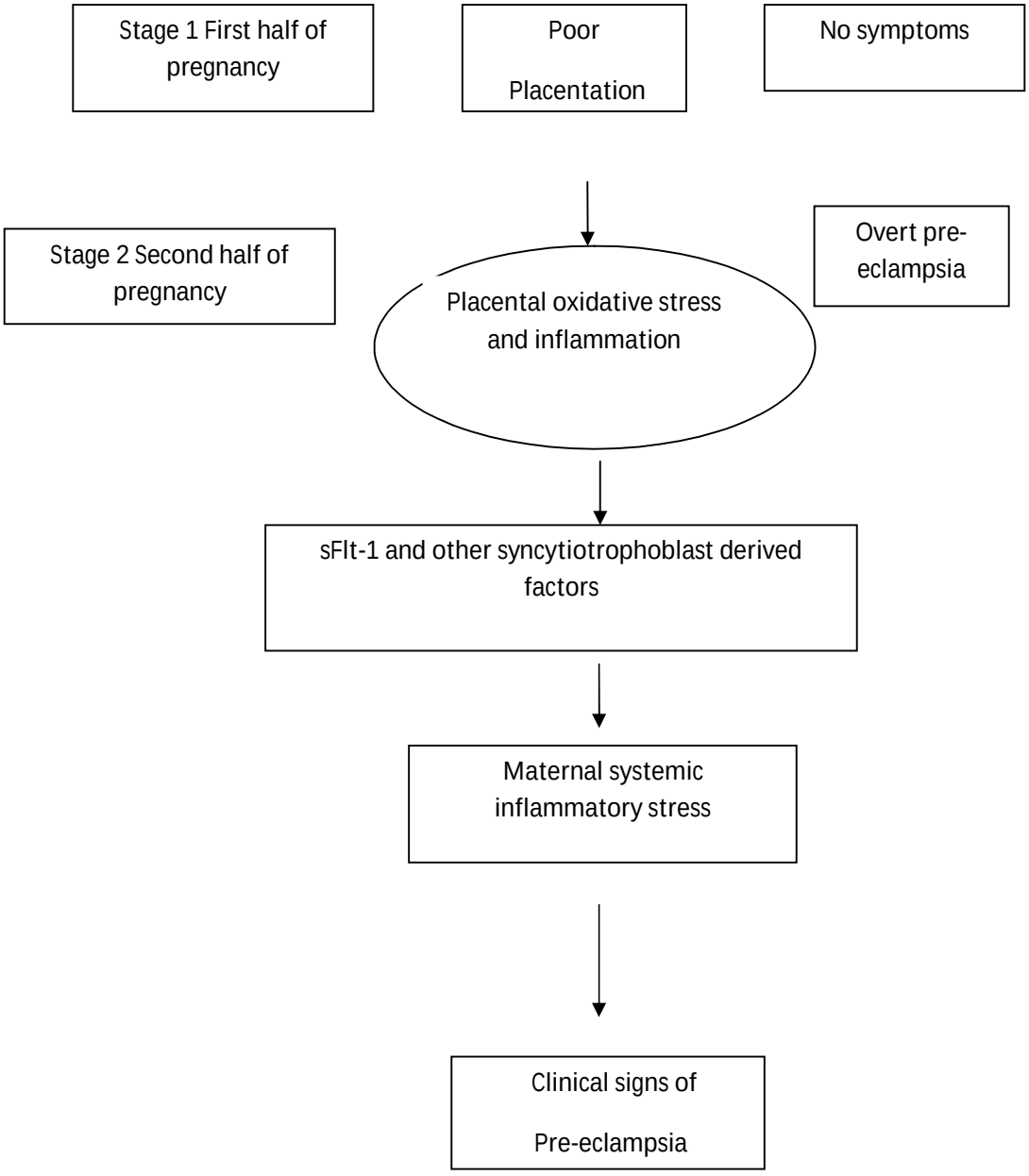
Pregnancy imposes a substantial systemic inflammatory stress on all pregnant women in the second half of pregnancy. The inflammatory stimulus may arise from debris shed into maternal circulation from the syncytiotrophoblast which if excessive may signal danger to the maternal innate immune system[8,10].

The two stage model of preeclampsia envisages that preeclampsia arises in various ways including from placental ischemia reperfusion injury secondary to deficient placentation. Poor placentation defines the first stage which would appear to have a different origin. The first stage decidual immune response account for the primipaternity & possible partner specificity of preeclampsia [4, 5].

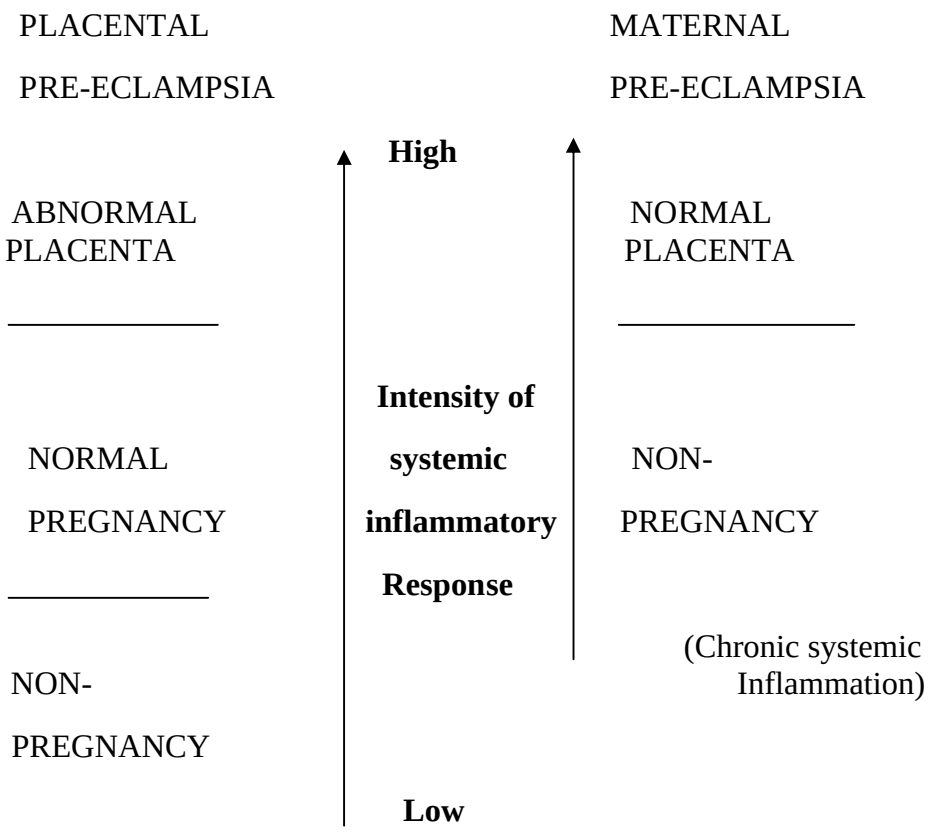
Second stage response all secondary to the systemic inflammatory response could also explain why women bearing pregnancies with unusually large placenta are susceptible to preeclampsia.

Any factor enhancing this response would predispose to preeclampsia. Indeed recent studies have shown that not only auto immune disorder but also certain maternal infection are involved in the etiology[15,17,18].

THE TWO STAGES OF PRE-ECLAMPSIA



TWO STAGE THEORY OF PRE-ECLAMPSIA



The flowchart depicts that in a completely normal woman although normal pregnancy stimulates a systemic response, it is not intense enough to cause preeclampsia. To do that requires the abnormal stimulus from oxidatively stressed placenta (Placental Preeclampsia).In a woman with chronic systemic inflammatory response associated condition like chronic hypertension, diabetes, etc ,the starting point is abnormal enough that each normal placenta can stimulate a systemic response of intensity to cause preeclampsia(Maternal Preeclampsia).

ENDOTHELIAL CELL ACTIVATION

The endothelium is one of the key organs involved in the pathophysiology of preeclampsia as evidenced by the prostacyclin (PGI2) thromboxane (TXA_2) imbalance, impairment of nitric oxide – cyclic guanosine monophosphate pathway & series of markers indicating endothelial activation. Glomerular endotheliosis but also ultrastructural changes in the placental bed & uterine boundary vessels, provides morphologic evidence of endothelial cell injury.

Endothelial cell activation fits the selective platelet activation and consumption & the resulting reduction in uteroplacental blood flow due to spiral artery thrombosis & placental infarction. Absence of normal stimulation of the renin angiotensin system despite relative hypovolemia in severe preeclampsia, increased vascular sensitivity to vasoconstrictors & increased endothelial cell permeability occur due to endothelial cell activation. An inadequate production of PGI_2 or NO or increased TXA_2 & serotonin also occur due to this[47, 50, 53, 54].

IMPAIRED CYTOTROPHOBLAST INVASION IN SPIRAL ARTERIES

In normal pregnancies endovascular cytotrophoblasts replace endothelial cells in the spiral arteries, this invasion results in destruction of the medial elastic, muscular & neural tissue. These so called physiologic changes normally reach the inner third of the myometrium.

Uterine natural killer (NK) cells produce a series of cytokines involved in angiogenesis and vascular stability including vascular endothelial growth factor (VEGF),placental growth factor (PLGF) and angiopoietin 2 and play a pivotal role in regulating trophoblastic invasion & maternal placental bed vascular changes[7,9,23,24,40].

In hypertensive pregnancies physiologic changes in many but not all spiral arteries are confined to the decidual portion of the arteries. In these arteries, the myometrial segments remain anatomically intact, do not dilate & the adrenergic nerve supply to the spiral arteries remains intact. Acute atherosis characterized by fibrinoid necrosis of vessel wall with an accumulation of lipid laden macrophages is commonly seen[25,41,44,53].

PRO AND ANTIANGIOGENIC PROTEINS

VEGF & PLGF induce vasodilator autacoids including NO & PGI_2 in endothelial cells & play a major role in pregnancy associated vasodilation & increase in GFR. VEGF &PLGF are produced by villous, extravillous CTB, STB & decidual leucocytes. The receptors for VEGF fms like tyrosine kinase – 1& kinase insert domain containing receptors are both expressed on human trophoblast in addition to endothelial cells[32,34,35,47].

VEGF is upregulated by hypoxia & provide an important mechanism through which the placenta develops according to metabolic requirements. PLGF is downregulated by hypoxia. sFlt-1, a soluble version of VEGF receptor generated by alternative splicing of Flt-1 gene is a major endogenous angiogenesis inhibitor because it retains the ability to bind to VEGF & PLGF while preventing VEGF & PLGF binding to cell surface receptors. The subsequent deficiency of free VEGF & PLGF leads to a state of endothelial dysfunction[48,49,53].

A novel soluble form of endoglin of placental origin present in sera of pregnant women is elevated in preeclampsia & amplifies endothelial dysfunction. A recent development was discovery of sFlt-14[33,39].

IMMUNOLOGICAL BASIS

The invasion of trophoblast into the deciduas & myometrium appears to be primarily controlled by immune mechanisms. STB do not express HLA antigen. CTB expresses HLA-G & HLA-E. It was thought that HLA-G offered maternal tolerance to fetus through failing to be perceived as foreign while still protecting from NK cell mediated cytotoxicity[34] .

Decidua predominantly contains NK cells. NK cells express inhibitory and activatory killer cell immunoglobulin like receptors (KIRS) capable of recognizing HLA class I molecules. All women express KIRs on decidual NK cells for HLA-C alleles & because HLA-C is polymorphic, each pregnancy will involve different combinations of paternally derived fetal HLA-C & maternal KIRs .Therefore each pregnancy is based on a unique couple specific immune interaction not necessarily involving T cells but NK cells interacting with paternal HLA. Mothers belonging to HLA-C2 group & lacking most or all activating KIRs when fetus has HLA-C are at risk of preeclampsia[53].

Regulatory T cells are also involved in specific immune tolerance. Sexual intercourse provokes a cascade of inflammatory response. TGF-beta 1 is the critical seminal factor which initiates a type 2 immune response. This prevents the induction of type 1 response against semiallogenic conceptus that are associated with poor placental & fetal development[35,39].

PLACENTAL ISCHEMIA/ PLACENTAL DEBRIS HYPOTHESIS

Increased deportation of placental tissue in future preeclamptics is already detectable at 16 to 18 weeks. The increased STB deportation is explained by the presence of syncytial sprouds that may be elongated on long pedicles. Apoptosis plays a central role in the formation of STB from underlying villous CTB. Apoptosis is increased in preeclampsia.

The maternal inflammatory response is the likely cause of the increased apoptosis. In earlier stages, increased apoptosis is caused by TNF, INF-gamma, FAS ligand later on caused by placental ischemia, reperfusion[33,42,43].

GENETIC CONFLICT HYPOTHESIS

According to Haigs genetic conflict theory fetal genes will be selected to increase the transfer of nutrients to the fetus and maternal genes will be selected to limit transfers. Genomic imprinting means that within fetal cells a similar conflict exists between genes that are maternally derived & genes that are paternally derived[28,30]. Placental factors (fetal genes) will act to increase maternal BP whereas maternal factors will act to reduce BP. This theory predicts that fetal genes will enhance flow of maternal blood through the intervillous space by increasing maternal BP (perfusion pressure)[51,52,53].

PREDICTION OF HYPERTENSION IN PREGNANCY

A review of world literature reveals that more than 100 clinical, biophysical & biochemical tests have been recommended to predict or identify the patient at risk. The results of the pooled data for the various tests & the lack of agreement between serial tests suggest that none of these clinical tests is sufficiently reliable for use as screening.

The biochemical markers were generally chosen on the basis of specific pathophysiologic abnormalities that cause preeclampsia. Hence markers of placental dysfunction, endothelial & coagulation activation, angiogenesis & systemic inflammation are used. The research in this aspect is still going on[27,31,32].

PREVENTIVE ASPECTS

There are numerous clinical trials describing the use of various methods to prevent or reduce the incidence of preeclampsia. Because the etiology of the disease is unknown these interventions have been used in an attempt to correct theoretical abnormalities[35,36,37]. In short randomized trials have evaluated protein, salt restriction, zinc, magnesium, fish oil, antioxidant supplementation, use of aspirin, heparin to prevent hypertension is pregnancy.

HOMOCYSTEINE

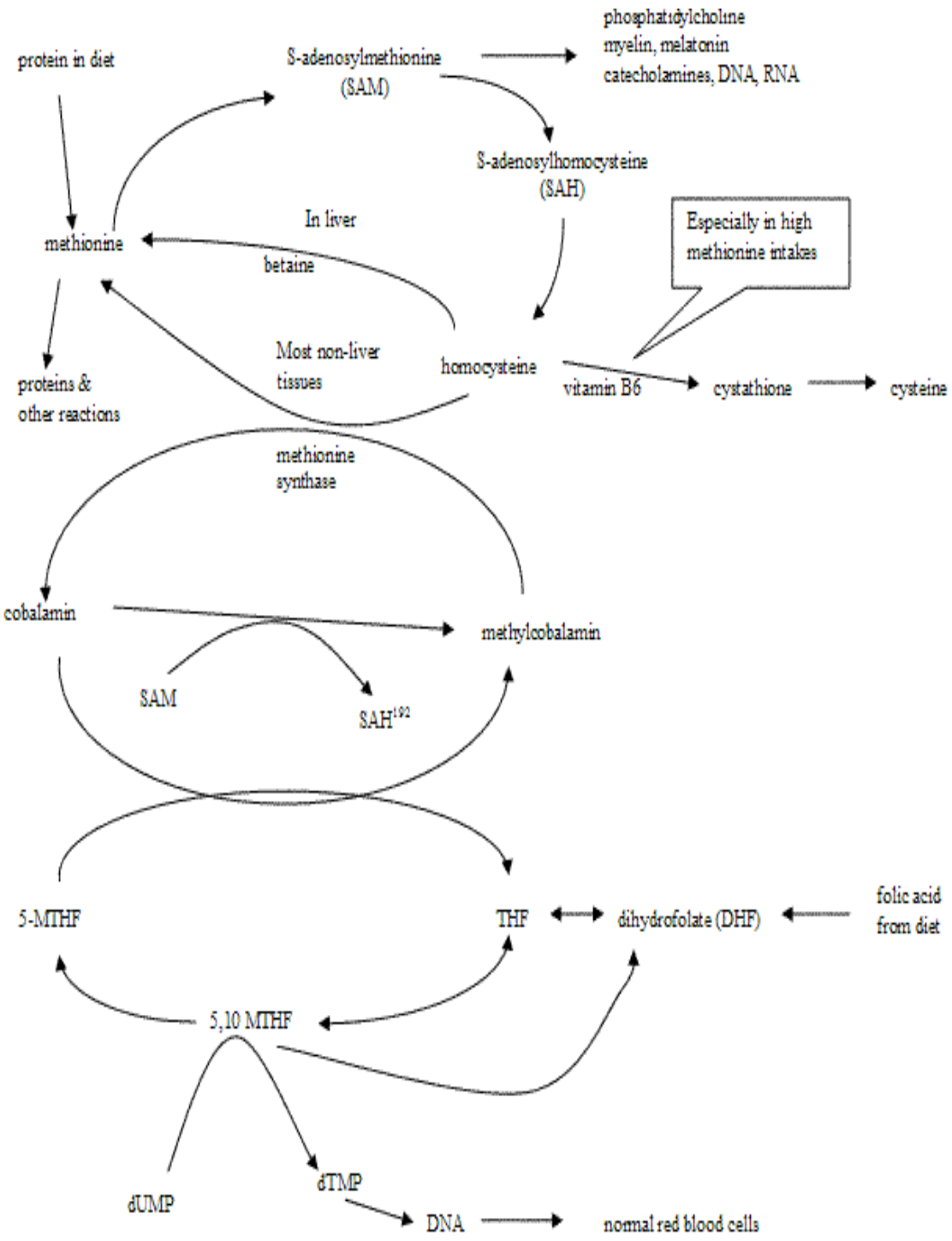
- Homocysteine is a non protein sulphur containing amino acid with the formula HSCH2 CH2 CH (NH2) CO2H.
- Homologue of the amino acid cysteine differing by an additional methylene group.
- It is biosynthesized from methionine by removal of terminal C methyl group
- It can be recycled into methionine or converted to cysteine.
- It exists at neutral PH values as zwitterions[55,56].

BIOSYNTHESIS & BIOCHEMICAL ROLES

Homocysteine is not obtained from the diet. Instead it is biosynthesized from methionine in a multiple step process. First methionine receives an adenosine group from ATP, a reaction catalyzed by adenosyl methionine synthetase to give rise to s-adenosyl methionine. SAM then transfers the methyl group to an acceptor molecule. The adenosine is then hydrolyzed to yield L-Homocysteine .L- Homocysteine has two primary fates.

1. Conversion to L-methionine
2. Conversion to L-cysteine[59,60,61]

BIOSYNTHESIS & BIOCHEMICAL ROLES OF HOMOCYSTEINE



BIOSYNTHESIS OF CYSTEINE

Mammals biosynthesis the amino acid cysteine via Homocysteine. Cystathionine beta synthase catalyses the condensation of Homocysteine & serine to give Cystathionine. This reaction uses pyridoxine (vit B6) as a cofactor. Cystathionine beta lyase then converts this double amino acid to cysteine, ammonia & alpha ketobutyrate.

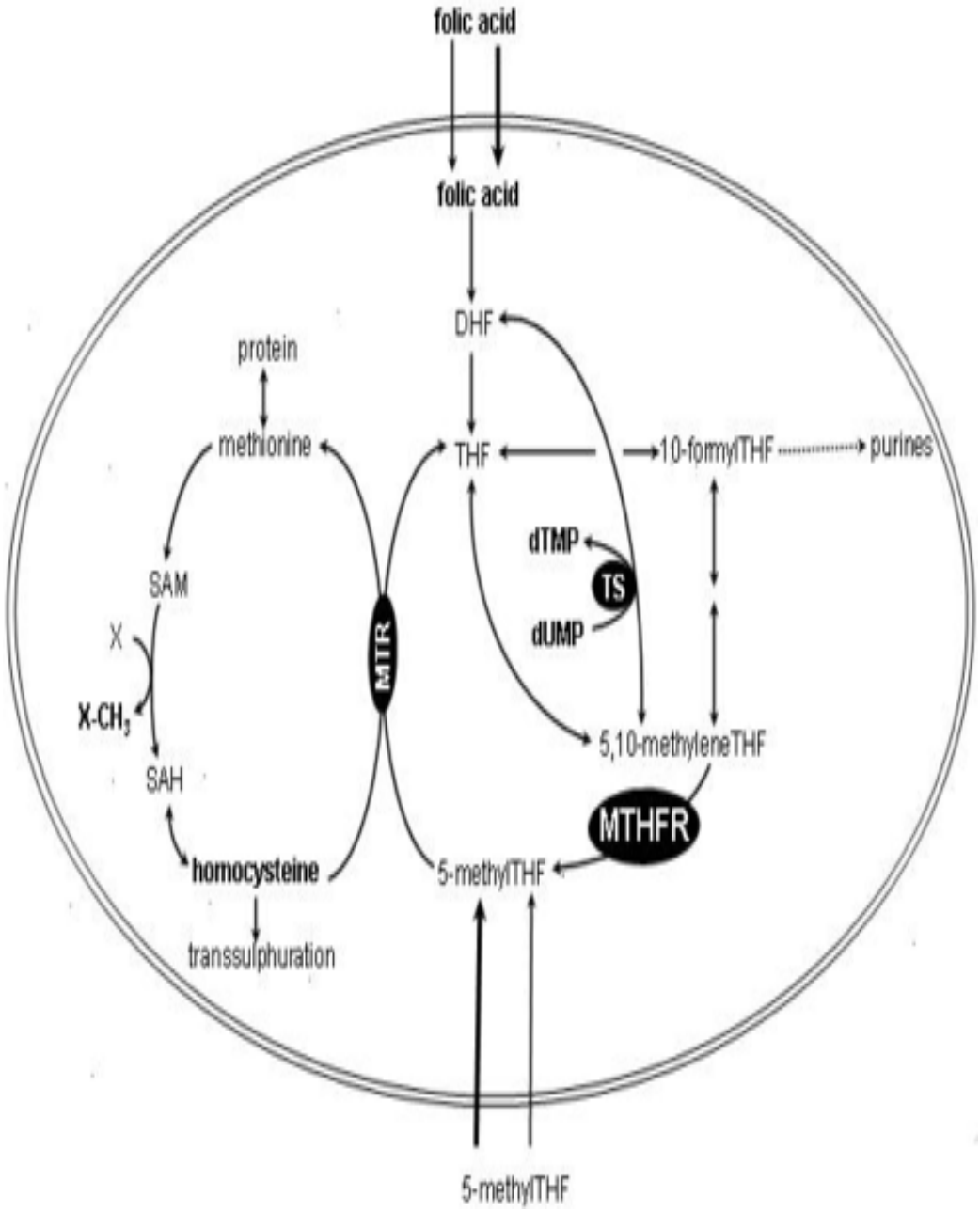
METHIONOINE SALVAGE

Homocysteine is remethylated by methyl tetrahydrofolate catalyzed by methionine synthase, a vitamin B12 dependent enzyme.

FOLATE TRAP

As the reduction of methylene tetrahydrofolate to methyl tetrahydrofolate is irreversible & the major source of tetrahydrofolate for the tissues is methyl THF, the role of methionine synthase is vital & provides the link between the functions of folate and vitamin B12. Impairment of methionine synthase in vitamin B12 deficiency results in the accumulation of methyl THF- the folate trap[59,60,61].

FOLATE TRAP



As depicted above the enzyme MTHFR is essential to convert 5, 10, methylene THF to methyl THF which is essential for conversion of homocysteine into methionine.

RISKS OF HYPERHOMOCYSTEINEMIA

Homocysteine degrades & inhibits the formation of the three main structural components of the artery- collagen, elastin and proteoglycans. It permanently degrades cysteine disulphide bridges & lysine amino acid residues in proteins gradually affecting function and structure. Simply put it is a 'corrosive' of long living proteins. It is linked to high concentrations of endothelial asymmetric dimethylarginine which causes endothelial dysfunction [22,26].

Homocysteine injures endothelial lining of arteries and stimulates the growth of smooth muscle cells. Excess homocysteine can form homocysteine thiolactone, a highly reactive intermediate which thiolates free amino groups in LDL & causes them to aggregate and be endocytosed by macrophages. The lipid deposits form atheromas. It causes lipid oxidation & platelet aggregation. It inhibits NO indirectly by stimulating superoxide anion production from endothelial cells. It enhances atherogenicity of LP(a) by liberating free Apo(a) & in turn inhibits fibrinolysis. It is atherogenic & thrombophilic. Elevated homocysteine levels are implicated in coronary, cerebrovascular &

peripheral arterial disease, DVT, neural tube defects in fetus and preeclampsia[57,58].

HYPERHOMOCYSTEINEMIA

Elevations of Homocysteine are associated with defects in 3 genes

1. Cystathionine Beta synthase
2. MTHFR
3. Methionine synthase

Of these the first two are clinically important. CBS gene defects leads to hyperhomocysteinemia & homocystinuria. MTHFR gene defects lead only to hyperhomocysteinemia. Heterozygotes do not have any manifestations. Homozygotes have clinical manifestations. The thermolabile variant of MTHFR is quite common.

It is also raised in early cobalamin & folate deficiency, chronic renal disease, alcoholism, smoking, vit B6 deficiency, hypothyroidism, therapy with steroids, cyclosporine. Levels are also

higher in serum than in plasma, in men than in women, in women on HRT/OCP, in elderly persons[55,56].

PLASMA HOMOCYSTEINE LEVELS

NORMAL - 5-15 µmol/L

HYPERHOMOCYSTEINEMIA

MILD - 15-25 µmol/L

MODERATE - 25-50 µmol/L

SEVERE - >50 µmol/L

Noto et al[62](2003) conducted a study in which Homocysteine levels were determined with chromatography on HPLC between the 20th & 24th week of pregnancy in women with analogous characteristics a) normotensive, b) with pregnancy induced hypertension, low, medium, high risk. Risk group was based on classification adopted by World Health Organization based on pressure data & coexistence of risk factors. The group they belonged to was confirmed after delivery. Homocysteine levels in normotensive pregnant women were low. Significant high levels of homocysteine present proportionally to the risk

degree of PIH. Higher levels of Homocysteine statistically significant were present in all risk groups.

Steegers Theunissen et al [68] (2004) conducted a study to assess associations between vitamin dependent Homocysteine metabolism and vascular related pregnancy complications by considering interval between delivery and postpartum investigation and maternal age. It was found hyperhomocysteinemia was associated with an approximately 2 fold to 3 fold increased risk for PIH, abruption & IUGR. Cobalamin deficiency was associated with HELLP syndrome, abruptio placenta, IUGR & IUD. Pyridoxal 5 phosphate deficiency increased risk of PIH. These associations lost the significance after adjustment for time interval & maternal age. High red cell folate was associated with a decreased risk for abruptio placentae and IUGR. An increased creatinine concentration was associated with PIH, preeclampsia, HELLP & abruption.

El abd et al [69](2009) determined the association between plasma homocysteine level and early onset severe preeclampsia and its relevance as a potential marker for predicting preeclampsia. Case control study was conducted on twenty early onset severe preeclamptic pregnant women and 10 normotensive pregnant women as controls. It was found

that plasma homocysteine significantly increased in early onset severe preeclampsia and it might contribute in the pathophysiology of the disease

Vincent et al[71] (2009) conducted a study in Nigeria. A total of 150 subjects consisting of 100 primigravidae & 25 diagnosed cases of pre-eclampsia/eclampsia and 25 non pregnant females were enrolled in the study. There was positive and significant correlation between plasma homocysteine in the eclamptic group & mean MCV & between plasma homocysteine, systolic & diastolic blood pressure of the eclamptic group.

Raijmakers et al[63](2001) investigated the role of Hyperhomocysteinemia in preeclampsia by measuring plasma levels of homocysteine and studying the prevalence of 677(C->T) polymorphism in the 5-10 MTHFR gene. Plasma samples of 10 healthy non pregnant women, 10 normotensive pregnant women & 20 women with preeclampsia were analysed for homocysteine levels.

Furthermore 167 non pregnant women previously hospitalized for preeclampsia and 403 population based controls were analyzed for 677(C->T) polymorphism. It was found in normotensive pregnancy homocysteine levels were lower compared with levels in

healthy non pregnant controls .Women with preeclampsia showed higher concentration of homocysteine. There was no difference in 677(C->T) polymorphism in preeclampsia and normal women.

Powers et al[64] (2001) conducted a study to confirm that endothelial dysfunction is present in preeclampsia and absent in transient hypertension of pregnancy & to determine whether homocysteine is associated with the degree of endothelial dysfunction in 17 women with preeclampsia, 16 women with transient hypertension of pregnancy & 34 normal pregnant women. It was concluded that cellular fibronectin was found to be significantly increased in women with preeclampsia compared to subjects with transient hypertension of pregnancy or normal pregnant women. Similarly plasma homocysteine was also significantly increased in women with preeclampsia compared to others. There was no apparent association between cellular fibronectin and homocysteine.

Sanchez et al[65](2001) measured maternal third trimester plasma folate, vitamin B12 and homocysteine concentration among 125 women with preeclampsia and 179 normotensive women. It was found that lower levels of folate, higher levels of homocysteine were associated

with preeclampsia. There was no association between low vitamin B12 levels and preeclampsia.

Lopez et al[67] (2003) conducted a study to determine possible association between hyperhomocysteinemia and preeclampsia. It was a case control study with 32 preeclamptics and 64 controls without pregnancy complications .Plasma total homocysteine determined by HPLC. Pregnant women with hyperhomocysteinemia have a 7.7 fold risk for preeclampsia was the conclusion arrived.

Materials and Methods

MATERIALS AND METHODS

Our study was a case control study. The cases of our study were postnatal patients who had gestational hypertension. The controls were postnatal patients who were comparable with the patients' groups with regard to social class, geographical area and age. They were friends or acquaintances of the patients and had uncomplicated pregnancies.

From October 2009 to November 2010 our study was conducted in the department of Obstetrics and Gynaecology, Coimbatore medical college hospital, Coimbatore on 111 patients. Gestational hypertension was defined as systolic BP> 140mm Hg & diastolic BP> 90mm Hg detected for the first time during pregnancy after 20 weeks of gestation. Preeclampsia was defined as gestational hypertension with proteinuria. Eclampsia defined as seizures that cannot be attributed to other causes in a woman with preeclampsia. Proteinuria is defined as >1+ dipstick.

For the measurement of BP, conventional sphygmomanometer was used. BP was measured after it was made sure that the women were relaxed & resting for at least half an hour before blood pressure measurement. It was measured in the sitting position with the forearm horizontal & well supported and the upper arm at the level of the heart. The cuff was long enough to encircle the arm and wide enough to cover at least two thirds of the upper arm. The disappearance of korotkoff phase V was used to define diastolic pressure. Two measurements at least 6 hours apart were taken. Mean arterial pressure is defined as systolic BP + 2/3 diastolic BP.

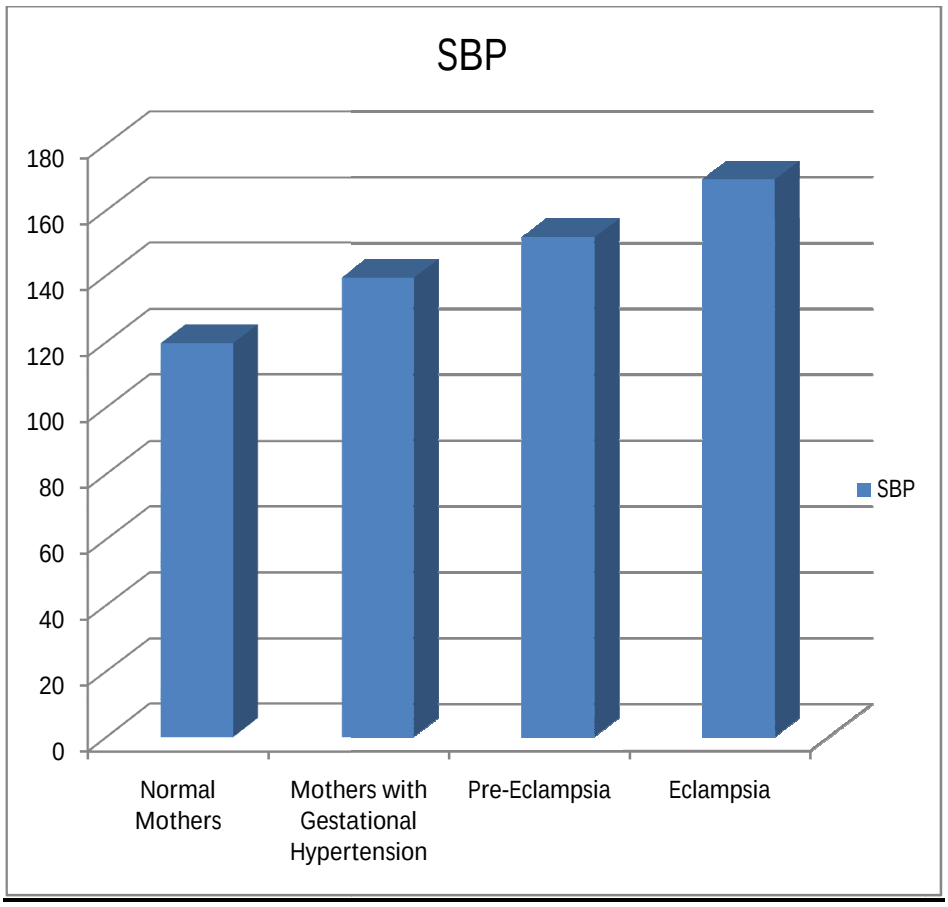
All participants were explained about the study and consent was obtained. After exclusion of users of vitamin B, folic acid, pharmacologic agents, restricted diets, women with disorder like chronic hypertension, diabetes mellitus, gastrointestinal, endocrine disorder, twin pregnancies, the study group consisted of 50 cases & 61 controls. Of the cases 16 had gestational hypertension, 26 had preeclampsia and 8 had Eclampsia. Controls had uncomplicated obstetric histories. The participants were subjected to detailed history elicitation & physical examination.

Peripheral blood sample was obtained from all participants in fasting state. The samples kept in cooled down polyethylene test tube containing EDTA (5µM/ml of blood) were immediately put into a freezer at -20 degree C, later to be used in dosing homocysteine. The blood sample was obtained within a day of delivery. The dosage of plasma homocysteine was carried out with Chemi luminescence immunoassay method. The normal range was between 5 and 15 µmol/L.

Results and Analysis

FIGURE-1

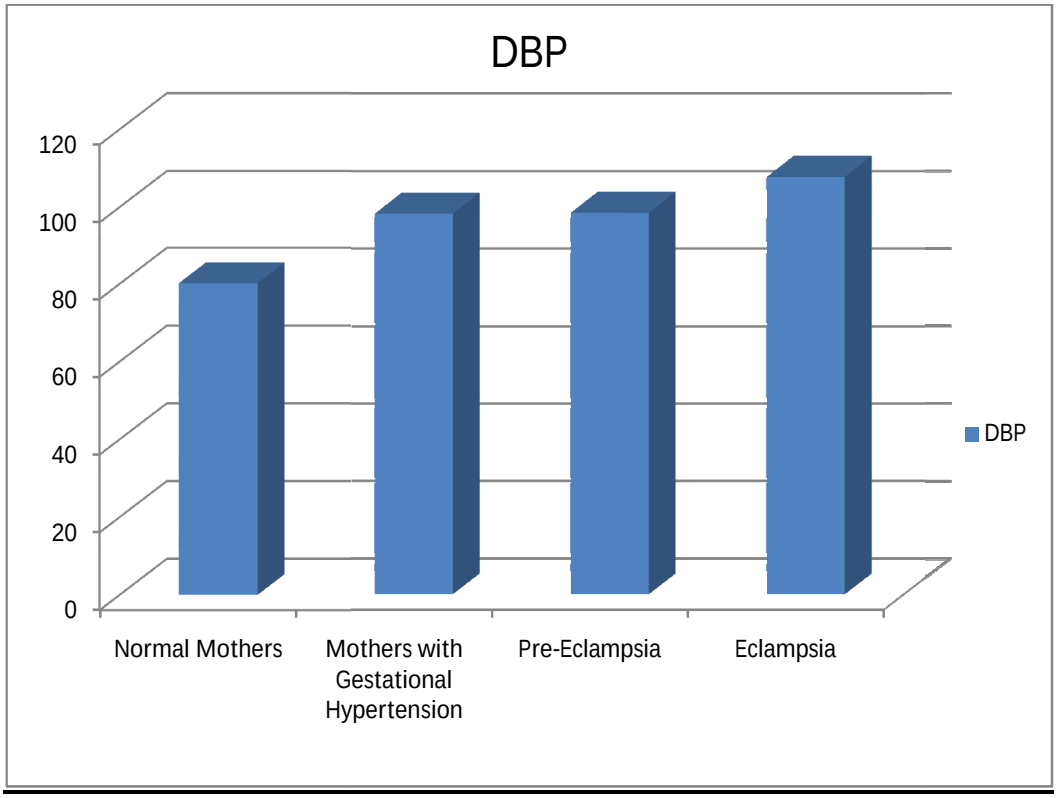
DISTRIBUTION OF SYSTOLIC BLOOD PRESSURE BETWEEN NORMAL MOTHERS AND MOTHERS WITH GESTATIONAL HYPERTENSION



The figure shows that mean SBP in normal mothers is 119.67mmHg, in mothers with gestational hypertension is 139.38mmHg, in preeclampsia is 151.69mmHg and in Eclampsia is 169.25mmHg.

FIGURE-2

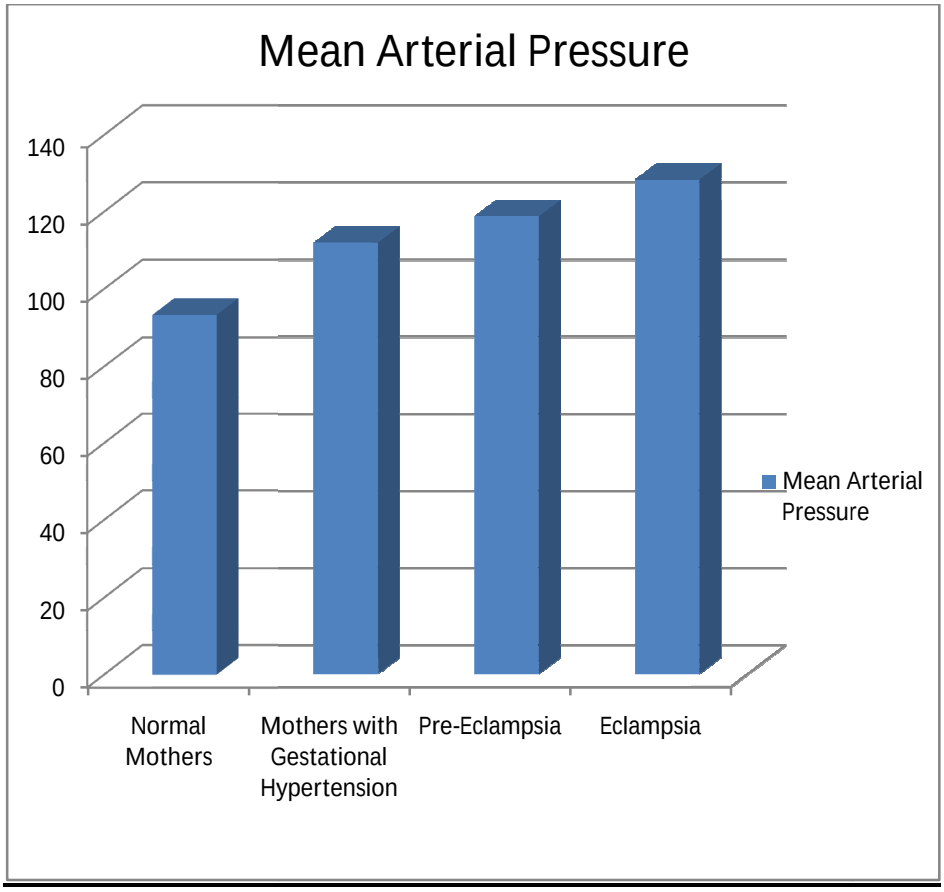
DISTRIBUTION OF DIASTOLIC BLOOD PRESSURE BETWEEN NORMAL MOTHERS AND MOTHERS WITH GESTATIONAL HYPERTENSION



The figure shows that mean DBP in normal mothers is 80.16 mmHg, in mothers with gestational hypertension is 98.13 mmHg, in preeclampsia is 98.38 mmHg and in Eclampsia is 107.75 mmHg.

FIGURE-3

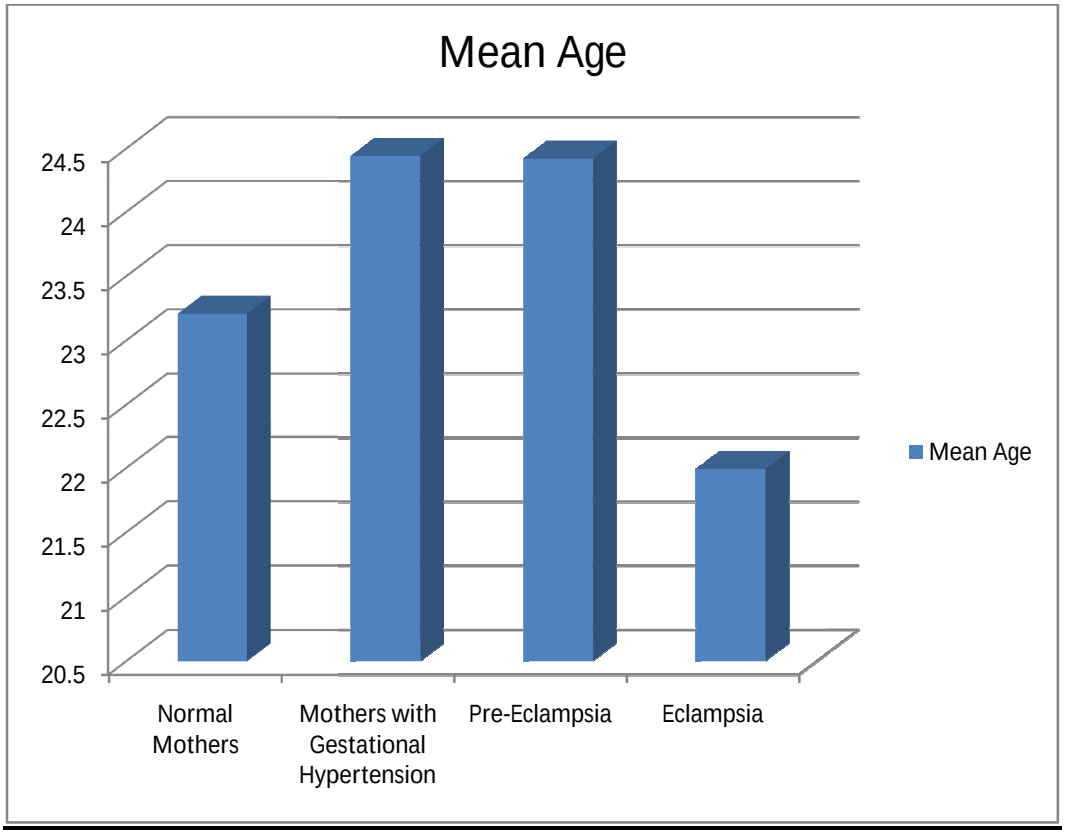
DISTRIBUTION OF MEAN ARTERIAL PRESSURE BETWEEN NORMAL MOTHERS AND MOTHERS WITH GESTATIONAL HYPERTENSION



The figure shows that mean MAP in normal mothers is 93.33 mmHg, in mothers with gestational hypertension is 111.88 mmHg, in preeclampsia is 118.72 mmHg and in Eclampsia is 128.25mmHg.

FIGURE-4

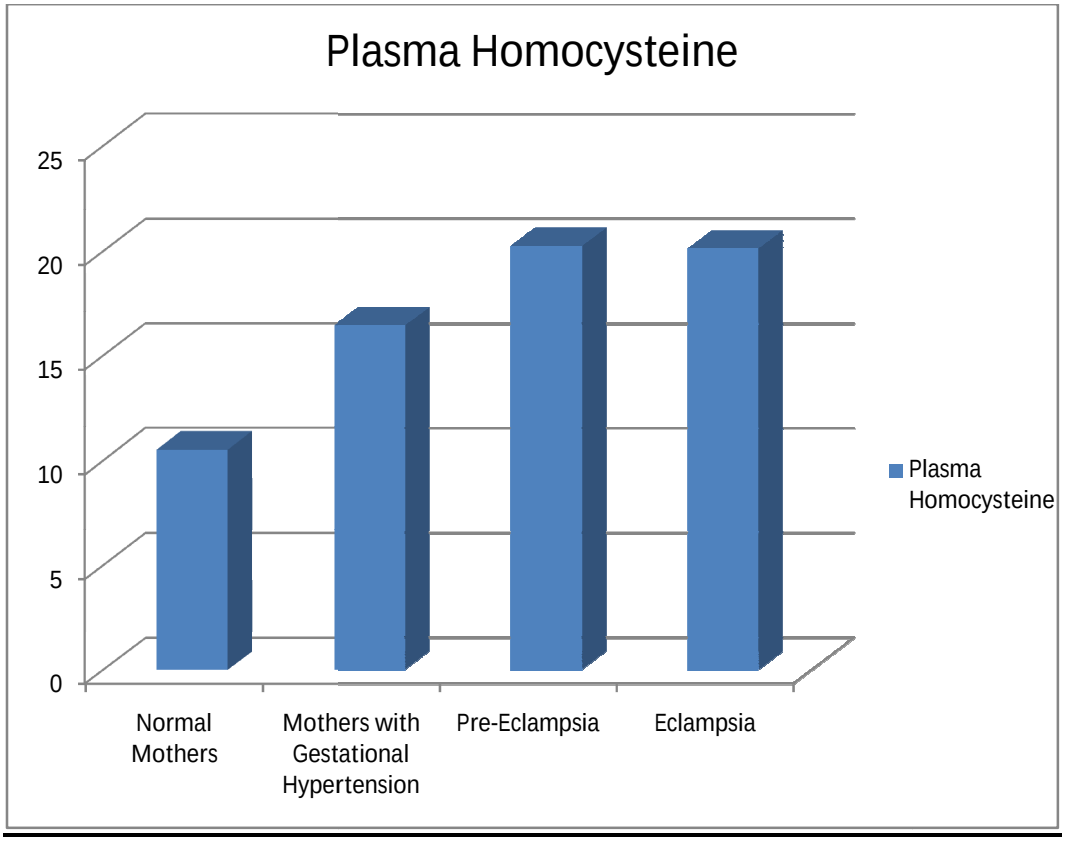
DISTRIBUTION OF AGE BETWEEN NORMAL MOTHERS AND MOTHERS WITH GESTATIONAL HYPERTENSION



The figure shows that mean age in normal mothers is 23.21 years, in mothers with gestational hypertension is 24.44 years, in preeclampsia is 24.42 years and in Eclampsia is 22 years

FIGURE-5

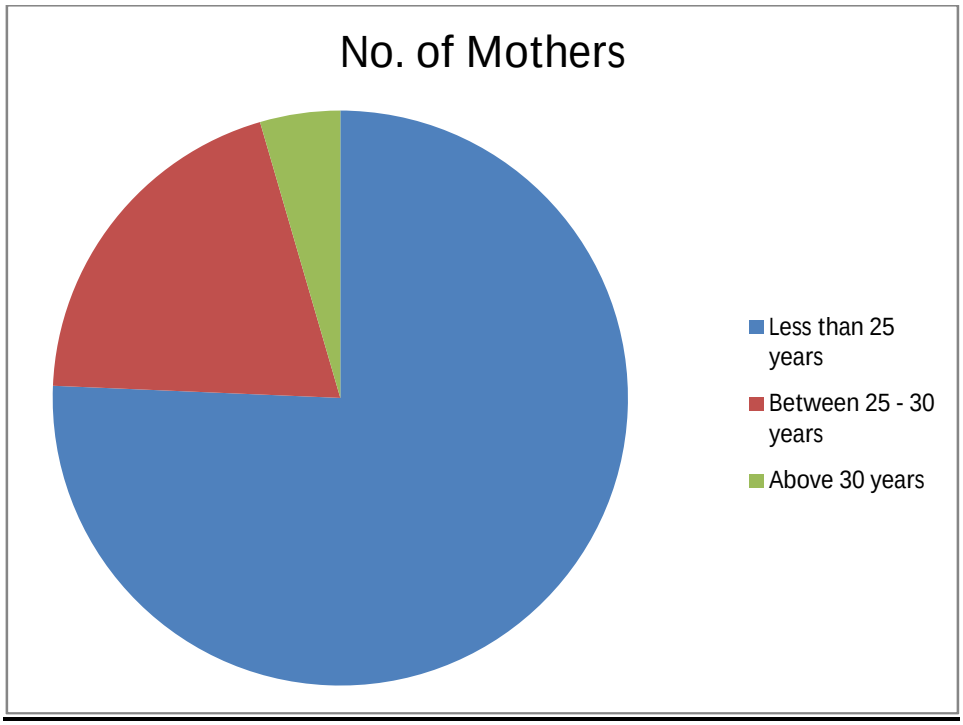
DISTRIBUTION OF PLASMA HOMOCYSTEINE BETWEEN NORMAL MOTHERS AND MOTHERS WITH GESTATIONAL HYPERTENSION



The figure shows that mean plasma homocysteine in normal mothers is 10.50µmol/L, in mothers with gestational hypertension is 16.43µmol/L, in preeclampsia is 20.23µmol/L and in Eclampsia is 20.10µmol/L.

FIGURE-6

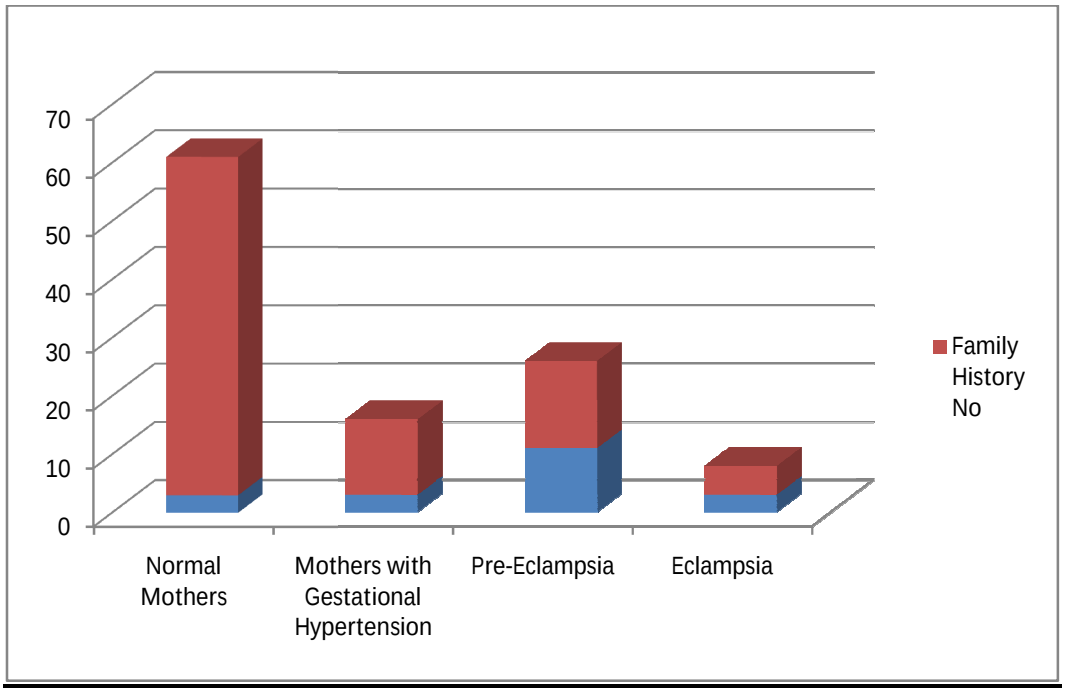
DISTRIBUTION OF AGE



It is inferred from the figure that of the total 111 participants 84 of them are in the age group < 25 years, 22 of them are in the age group between 25-30 years and 5 of them are in the age group above 30 years.

FIGURE-7

ASSOCIATION BETWEEN FAMILY HISTORY OF CARDIOVASCULAR DISEASE AND GESTATIONAL HYPERTENSION



The figure depicts that positive family history of cardiovascular disease is found more in mothers with gestational hypertension, preeclampsia and Eclampsia than in normal mothers.

TABLE-1

DESCRIPTIVE STATISTICS

	N	Minimum	Maximum	Mean	Std. Deviation
Age	111	18	38	23.59	3.602
SBP	111	110	180	133.59	17.666
DBP	111	70	130	89.01	15.523
Mean Arterial Pressure	111	83.33	176.67	104.4685	15.07492
Birth Weight of Child	111	1.40	3.70	2.8080	.34712
P.Homocysteine	111	6	54	14.32	7.899
Valid N (list wise)	111				

The table shows the minimum, maximum, mean and standard deviation values of all variables.

TABLE-2

ASSOCIATION BETWEEN AGE AND GESTATIONAL HYPERTENSION

			Diagnosis				
			Normal	Gestational Hypertension	Pre Eclampsia	Eclampsia	Total
Age	Less than 25 years	Count	48	11	18	7	84
		% within Age	57.1%	13.1%	21.4%	8.3%	100.0%
		% within Diagnosis	78.7%	68.8%	69.2%	87.5%	75.7%
	Between 25 - 30 years	Count	12	3	6	1	22
		% within Age	54.5%	13.6%	27.3%	4.5%	100.0%
		% within Diagnosis	19.7%	18.8%	23.1%	12.5%	19.8%
	Above 30 years	Count	1	2	2	0	5
		% within Age	20.0%	40.0%	40.0%	.0%	100.0%
		% within Diagnosis	1.6%	12.5%	7.7%	.0%	4.5%
Total		Count	61	16	26	8	111
		% within Age	55.0%	14.4%	23.4%	7.2%	100.0%
		% within Diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%

The Chi square value of age and gestational hypertension is 5.160 and p= 0.523, so it can be inferred that there is no association between the two.

TABLE-3

ASSOCIATION BETWEEN PARITY AND GESTATIONAL HYPERTENSION

			Diagnosis				
			Normal	Gestational Hypertension	Pre Eclampsia	Eclampsia	Total
Parity	One	Count	32	11	16	7	66
		% within Parity	48.5%	16.7%	24.2%	10.6%	100.0%
		% within Diagnosis	52.5%	68.8%	61.5%	87.5%	59.5%
	Two	Count	25	5	5	1	36
		% within Parity	69.4%	13.9%	13.9%	2.8%	100.0%
		% within Diagnosis	41.0%	31.3%	19.2%	12.5%	32.4%
	Three	Count	3	0	4	0	7
		% within Parity	42.9%	.0%	57.1%	.0%	100.0%
		% within Diagnosis	4.9%	.0%	15.4%	.0%	6.3%
	Four	Count	1	0	1	0	2
		% within Parity	50.0%	.0%	50.0%	.0%	100.0%
		% within Diagnosis	1.6%	.0%	3.8%	.0%	1.8%
Total		Count	61	16	26	8	111
		% within Parity	55.0%	14.4%	23.4%	7.2%	100.0%
		% within Diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%

The Chi square value of parity and gestational hypertension is 11.713 and p= 0.230, so it can be inferred that there is no association between the two.

TABLE-4

ASSOCIATION BETWEEN No. OF LIVE BIRTHS AND GESTATIONAL HYPERTENSION

			Diagnosis				
			Normal	Gestational Hypertension	Pre Eclampsia	Eclampsia	Total
Live	Nil	Count	0	3	1	2	6
		% within Live	.0%	50.0%	16.7%	33.3%	100.0%
		% within Diagnosis	.0%	18.8%	3.8%	25.0%	5.4%
	One	Count	33	7	17	5	62
		% within Live	53.2%	11.3%	27.4%	8.1%	100.0%
		% within Diagnosis	54.1%	43.8%	65.4%	62.5%	55.9%
	Two	Count	24	4	4	1	33
		% within Live	72.7%	12.1%	12.1%	3.0%	100.0%
		% within Diagnosis	39.3%	25.0%	15.4%	12.5%	29.7%
	Three	Count	3	2	3	0	8
		% within Live	37.5%	25.0%	37.5%	.0%	100.0%
		% within Diagnosis	4.9%	12.5%	11.5%	.0%	7.2%
	Four	Count	1	0	1	0	2
		% within Live	50.0%	.0%	50.0%	.0%	100.0%
		% within Diagnosis	1.6%	.0%	3.8%	.0%	1.8%
Total		Count	61	16	26	8	111
		% within Live	55.0%	14.4%	23.4%	7.2%	100.0%
		% within Diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%

The Chi square value of no of live births and gestational hypertension is 23.286 and $p < 0.05$, so it can be inferred that there is an association between the two.

TABLE-5

ASSOCIATION BETWEEN No. OF ABORTIONS AND GESTATIONAL HYPERTENSION

			Diagnosis				
			Normal	Gestational Hypertension	Pre Eclampsia	Eclampsia	Total
Abortion	Nil	Count	58	15	21	7	101
		% within Abortion	57.4%	14.9%	20.8%	6.9%	100.0%
		% within Diagnosis	95.1%	93.8%	80.8%	87.5%	91.0%
	One	Count	3	1	4	1	9
		% within Abortion	33.3%	11.1%	44.4%	11.1%	100.0%
		% within Diagnosis	4.9%	6.3%	15.4%	12.5%	8.1%
	Two	Count	0	0	1	0	1
		% within Abortion	.0%	.0%	100.0%	.0%	100.0%
		% within Diagnosis	.0%	.0%	3.8%	.0%	.9%
Total		Count	61	16	26	8	111
		% within Abortion	55.0%	14.4%	23.4%	7.2%	100.0%
		% within Diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%

The Chi square value of no of abortions and gestational hypertension is 6.426 and p= 0.377, so it can be inferred that there is no association between the two.

TABLE-6

ASSOCIATION BETWEEN MATERNAL BLOOD GROUPS AND GESTATIONAL HYPERTENSION

			Diagnosis				
			Normal	Gestational Hypertension	Pre Eclampsia	Eclampsia	Total
Blood Group	O+ve	Count	19	6	8	1	34
		% within Blood Group	55.9%	17.6%	23.5%	2.9%	100.0%
		% within Diagnosis	31.1%	37.5%	30.8%	12.5%	30.6%
	B+ve	Count	16	7	8	4	35
		% within Blood Group	45.7%	20.0%	22.9%	11.4%	100.0%
		% within Diagnosis	26.2%	43.8%	30.8%	50.0%	31.5%
	A+ve	Count	26	2	9	3	40
		% within Blood Group	65.0%	5.0%	22.5%	7.5%	100.0%
		% within Diagnosis	42.6%	12.5%	34.6%	37.5%	36.0%
	AB+ve	Count	0	1	1	0	2
		% within Blood Group	.0%	50.0%	50.0%	.0%	100.0%
		% within Diagnosis	.0%	6.3%	3.8%	.0%	1.8%
Total		Count	61	16	26	8	111
		% within Blood Group	55.0%	14.4%	23.4%	7.2%	100.0%
		% within Diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%

The Chi square value of maternal blood groups and gestational hypertension is 10.099 and p= 0.343, so it can be inferred that there is no association between the two.

TABLE-7

ASSOCIATION BETWEEN FAMILY HISTORY OF CARDIOVASCULAR DISEASE AND GESTATIONAL HYPERTENSION

			Diagnosis				
			Normal	Gestational Hypertension	Pre Eclampsia	Eclampsia	Total
Family History	No	Count	58	13	15	5	91
		% within Family History	63.7%	14.3%	16.5%	5.5%	100.0%
		% within Diagnosis	95.1%	81.3%	57.7%	62.5%	82.0%
	Yes	Count	3	3	11	3	20
		% within Family History	15.0%	15.0%	55.0%	15.0%	100.0%
		% within Diagnosis	4.9%	18.8%	42.3%	37.5%	18.0%
Total		Count	61	16	26	8	111
		% within Family History	55.0%	14.4%	23.4%	7.2%	100.0%
		% within Diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%

The Chi square value of family history of cardiovascular disease and gestational hypertension is 19.533 and $p < 0.001$, so it can be inferred that there is an association between the two.

TABLE-8

ASSOCIATION BETWEEN SEX OF CHILD AND GESTATIONAL HYPERTENSION

			Diagnosis				
			Normal	Gestational Hypertension	Pre Eclampsia	Eclampsia	Total
Child Sex	Male	Count	33	10	17	3	63
		% within Child Sex	52.4%	15.9%	27.0%	4.8%	100.0%
		% within Diagnosis	54.1%	62.5%	65.4%	37.5%	56.8%
	Female	Count	28	6	9	5	48
		% within Child Sex	58.3%	12.5%	18.8%	10.4%	100.0%
		% within Diagnosis	45.9%	37.5%	34.6%	62.5%	43.2%
Total		Count	61	16	26	8	111
		% within Child Sex	55.0%	14.4%	23.4%	7.2%	100.0%
		% within Diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%

The Chi square value of sex of child and gestational hypertension is 2.388 and p=0.496, so it can be inferred that there is no association between the two.

TABLE-9

ASSOCIATION BETWEEN BIRTH WEIGHT OF CHILD AND GESTATIONAL HYPERTENSION

			Diagnosis				
			Normal	Gestational Hypertension	Pre Eclampsia	Eclampsia	Total
Weight	Less than 2.5 Kg	Count	19	5	3	0	27
		% within Weight	70.4%	18.5%	11.1%	.0%	100.0%
		% within Diagnosis	31.1%	31.3%	11.5%	.0%	24.3%
	2.5 - 3 Kg	Count	28	9	20	7	64
		% within Weight	43.8%	14.1%	31.3%	10.9%	100.0%
		% within Diagnosis	45.9%	56.3%	76.9%	87.5%	57.7%
	Above 3 Kg	Count	14	2	3	1	20
		% within Weight	70.0%	10.0%	15.0%	5.0%	100.0%
		% within Diagnosis	23.0%	12.5%	11.5%	12.5%	18.0%
Total		Count	61	16	26	8	111
		% within Weight	55.0%	14.4%	23.4%	7.2%	100.0%
		% within Diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%

The Chi square value of birth weight of child and gestational hypertension is 11.389 and p=0.077, so it can be inferred that there is no association between the two.

TABLE-10

ASSOCIATION BETWEEN PLASMA HOMOCYSTEINE AND GESTATIONAL HYPERTENSION

			Diagnosis				
			Normal	Gestational Hypertension	Pre Eclampsia	Eclampsia	Total
Plasma Homocysteine	Normal	Count	57	8	9	2	76
		% within Plasma Homocysteine	75.0%	10.5%	11.8%	2.6%	100.0%
		% within Diagnosis	93.4%	50.0%	34.6%	25.0%	68.5%
	Abnormal	Count	4	8	17	6	35
		% within Plasma Homocysteine	11.4%	22.9%	48.6%	17.1%	100.0%
		% within Diagnosis	6.6%	50.0%	65.4%	75.0%	31.5%
Total		Count	61	16	26	8	111
		% within Plasma Homocysteine	55.0%	14.4%	23.4%	7.2%	100.0%
		% within Diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%

The Chi square value of plasma homocysteine and gestational hypertension is 40.954 and $p<0.001$, so it can be inferred that there is an association between the two.

TABLE-11

CORRELATION BETWEEN FACTORS

		Parity	Family History	MAP	SBP	DBP	P.Homocysteine
Parity	Pearson correlation(r) Significance(p) N.	1 111	098 .306 111	.042 .663 111	.089 .353 111	.111 .244 111	.010 .919 111
Family History	Pearson correlation(r) Significance(p) N.	.098 .306 111	1 111	.360** .000 111	438** .000 111	.276** .003 111	.181 .058 111
MAP	Pearson correlation(r) Significance(p) N.	042 .663 111	.360** .000 111	1 111	.872** .000 111	.960** .000 111 .	.447** .000 111
SBP	Pearson correlation(r) Significance(p) N.	.089 .353 111	438** .000 111	.872** .000 111	1 111	.701** .000 111	.559** .000 111
DBP	Pearson correlation(r) Significance(p) N.	.111 .244 111	.276** .003 111	.960** .000 111 .	.701** .000 111	1 111	.334** .000 111
P.Homocysteine	Pearson correlation(r) Significance(p) N.	010 .919 111	.181 .058 111	.477** .000 111	.559** .000 111	.334** .000 111	1 111

**correlation is significant at the 0.01 level

The table depicts the positive correlation between Family history of cardiovascular disease, SBP, DBP, MAP and plasma homocysteine.

TABLE-12

ASSOCIATION BETWEEN AGE AND PLASMA HOMOCYSTEINE

			Plasma Homocysteine		
			Normal	Abnormal	Total
Age	Less than 25 years	Count	57	27	84
		% within Age	67.9%	32.1%	100.0%
		% within Plasma Homocysteine	75.0%	77.1%	75.7%
	Between 25 - 30 years	Count	15	7	22
		% within Age	68.2%	31.8%	100.0%
		% within Plasma Homocysteine	19.7%	20.0%	19.8%
	Above 30 years	Count	4	1	5
		% within Age	80.0%	20.0%	100.0%
		% within Plasma Homocysteine	5.3%	2.9%	4.5%
Total		Count	76	35	111
		% within Age	68.5%	31.5%	100.0%
		% within Plasma Homocysteine	100.0%	100.0%	100.0%

The chi square value of age and plasma homocysteine is 0.323 and p=0.851, so it can be inferred that there is no association between the two.

TABLE-13

ASSOCIATION BETWEEN PARITY AND PLASMA HOMOCYSTEINE

			Plasma Homocysteine		
			Normal	Abnormal	Total
Parity	One	Count	43	23	66
		% within Parity	65.2%	34.8%	100.0%
		% within Plasma Homocysteine	56.6%	65.7%	59.5%
	Two	Count	27	9	36
		% within Parity	75.0%	25.0%	100.0%
		% within Plasma Homocysteine	35.5%	25.7%	32.4%
	Three	Count	4	3	7
		% within Parity	57.1%	42.9%	100.0%
		% within Plasma Homocysteine	5.3%	8.6%	6.3%
	Four	Count	2	0	2
		% within Parity	100.0%	.0%	100.0%
		% within Plasma Homocysteine	2.6%	.0%	1.8%
Total		Count	76	35	111
		% within Parity	68.5%	31.5%	100.0%
		% within Plasma Homocysteine	100.0%	100.0%	100.0%

The chi square value of parity and plasma homocysteine is 2.385 and p=0.496, so it can be inferred that there is no association between the two.

TABLE-14

ASSOCIATION BETWEEN No. OF LIVE BIRTHS AND PLASMA HOMOCYSTEINE

			Plasma Homocysteine		
			Normal	Abnormal	Total
Live	Nil	Count	3	3	6
		% within Live	50.0%	50.0%	100.0%
		% within Plasma Homocysteine	3.9%	8.6%	5.4%
	One	Count	42	20	62
		% within Live	67.7%	32.3%	100.0%
		% within Plasma Homocysteine	55.3%	57.1%	55.9%
	Two	Count	26	7	33
		% within Live	78.8%	21.2%	100.0%
		% within Plasma Homocysteine	34.2%	20.0%	29.7%
	Three	Count	3	5	8
		% within Live	37.5%	62.5%	100.0%
		% within Plasma Homocysteine	3.9%	14.3%	7.2%
	Four	Count	2	0	2
		% within Live	100.0%	.0%	100.0%
		% within Plasma Homocysteine	2.6%	.0%	1.8%
Total		Count	76	35	111
		% within Live	68.5%	31.5%	100.0%
		% within Plasma Homocysteine	100.0%	100.0%	100.0%

The chi square value of no of live births and plasma homocysteine is 7.066 and p=0.132, so it can be inferred that there is no association between the two.

TABLE-15

ASSOCIATION BETWEEN No. OF ABORTIONS AND PLASMA HOMOCYSTEINE

			Plasma Homocysteine		
			Normal	Abnormal	Total
Abortion	Nil	Count	71	30	101
		% within Abortion	70.3%	29.7%	100.0%
		% within Plasma Homocysteine	93.4%	85.7%	91.0%
	One	Count	5	4	9
		% within Abortion	55.6%	44.4%	100.0%
		% within Plasma Homocysteine	6.6%	11.4%	8.1%
	Two	Count	0	1	1
		% within Abortion	.0%	100.0%	100.0%
		% within Plasma Homocysteine	.0%	2.9%	.9%
Total		Count	76	35	111
		% within Abortion	68.5%	31.5%	100.0%
		% within Plasma Homocysteine	100.0%	100.0%	100.0%

The chi square value of no of abortions and plasma homocysteine is 3.023 and p=0.221, so it can be inferred that there is no association between the two.

TABLE-16

ASSOCIATION BETWEEN MATERNAL BLOOD GROUPS AND PLASMA HOMOCYSTEINE

			Plasma Homocysteine		
			Normal	Abnormal	Total
Blood Group	O+ve	Count	20	14	34
		% within Blood Group	58.8%	41.2%	100.0%
		% within Plasma Homocysteine	26.3%	40.0%	30.6%
	B+ve	Count	22	13	35
		% within Blood Group	62.9%	37.1%	100.0%
		% within Plasma Homocysteine	28.9%	37.1%	31.5%
	A+ve	Count	32	8	40
		% within Blood Group	80.0%	20.0%	100.0%
		% within Plasma Homocysteine	42.1%	22.9%	36.0%
	AB+ve	Count	2	0	2
		% within Blood Group	100.0%	.0%	100.0%
		% within Plasma Homocysteine	2.6%	.0%	1.8%
Total		Count	76	35	111
		% within Blood Group	68.5%	31.5%	100.0%
		% within Plasma Homocysteine	100.0%	100.0%	100.0%

The chi square value of maternal blood groups and plasma homocysteine is 5.360 and p=0.147, so it can be inferred that there is no association between the two.

TABLE-17

ASSOCIATION BETWEEN FAMILY HISTORY OF CARDIOVASCULAR DISEASE AND PLASMA HOMOCYSTEINE

			Plasma Homocysteine		
			Normal	Abnormal	Total
Family History	No	Count	66	25	91
		% within Family History	72.5%	27.5%	100.0%
		% within Plasma Homocysteine	86.8%	71.4%	82.0%
	Yes	Count	10	10	20
		% within Family History	50.0%	50.0%	100.0%
		% within Plasma Homocysteine	13.2%	28.6%	18.0%
Total		Count	76	35	111
		% within Family History	68.5%	31.5%	100.0%
		% within Plasma Homocysteine	100.0%	100.0%	100.0%

The chi square value of family history of cardiovascular disease and plasma homocysteine is 3.854 and $p<0.05$, so it can be inferred that there is an association between the two.

TABLE-18

ASSOCIATION BETWEEN SEX OF CHILD AND PLASMA HOMOCYSTEINE

			Plasma Homocysteine		
			Normal	Abnormal	Total
Child Sex	Male	Count	44	19	63
		% within Child Sex	69.8%	30.2%	100.0%
		% within Plasma Homocysteine	57.9%	54.3%	56.8%
	Female	Count	32	16	48
		% within Child Sex	66.7%	33.3%	100.0%
		% within Plasma Homocysteine	42.1%	45.7%	43.2%
Total		Count	76	35	111
		% within Child Sex	68.5%	31.5%	100.0%
		% within Plasma Homocysteine	100.0%	100.0%	100.0%

The Chi square value of sex of child and plasma homocysteine is 0.127 and p=0.721, so it can be inferred that there is no association between the two.

TABLE-19

ASSOCIATION BETWEEN BIRTH WEIGHT OF CHILD AND PLASMA HOMOCYSTEINE

			Plasma Homocysteine		
			Normal	Abnormal	Total
Weight	Less than 2.5 Kg	Count	23	4	27
		% within Weight	85.2%	14.8%	100.0%
		% within Plasma Homocysteine	30.3%	11.4%	24.3%
	2.5 - 3 Kg	Count	37	27	64
		% within Weight	57.8%	42.2%	100.0%
		% within Plasma Homocysteine	48.7%	77.1%	57.7%
	Above 3 Kg	Count	16	4	20
		% within Weight	80.0%	20.0%	100.0%
		% within Plasma Homocysteine	21.1%	11.4%	18.0%
Total		Count	76	35	111
		% within Weight	68.5%	31.5%	100.0%
		% within Plasma Homocysteine	100.0%	100.0%	100.0%

The Chi square value of birth weight of child and plasma homocysteine is 8.093 and $p<0.01$, so it can be inferred that there is an association between the two.

Discussion

DISCUSSION

Our study was conducted in the Department of Obstetrics and Gynaecology, Coimbatore Medical College hospital ,Coimbatore, of Tamilnadu Dr M.G.R. Medical university with the aim of finding a relationship between plasma homocysteine levels and gestational hypertension with 111 participants.

The results were expressed as means, standard deviation. For groups chi square test and the student t test were used. Pearson co-relation coefficient was used to detect the correlation between different variables. The level of significance was 0.05.

The mean age in the control group was 23.21 years, in mothers with gestational hypertension was 24.44 years, in preeclampsia was 24.42 years and in Eclampsia was 22 years as shown in figure-4. There was no significant difference between the groups as regards women's age . The mean SBP in normal mothers was 119.67mmHg, in mothers with gestational hypertension was 139.38mmHg, in preeclampsia

was 151.69mmHg and in Eclampsia was 169.25mmHg as shown in figure-1.The mean DBP in normal mothers was 80.16 mmHg, in mothers with gestational hypertension was 98.13 mmHg, in preeclampsia was 98.38 mmHg and in Eclampsia was 107.75 mmHg as shown in figure-2.

Mean MAP in normal mothers was 93.33 mmHg, in mothers with gestational hypertension was 111.88 mmHg, in preeclampsia was 118.72 mmHg and in Eclampsia was 128.25 mmHg as shown in figure-3. The mean SBP, DBP& MAP were significantly higher in cases than in controls.

Mean plasma homocysteine in normal mothers was 10.50µmol/L, in mothers with gestational hypertension was 16.43µmol/L, in preeclampsia was 20.23µmol/L and in Eclampsia was 20.10µmol/L as shown in figure-5. Mean Plasma homocysteine levels were found to be significantly higher in cases compared to controls.

In our study there was no significant association between age and gestational hypertension ($p=0.523$,table-2) and also no association between parity and gestational hypertension($p=0.230$,table-3). There were significant associations between live births and gestational hypertension ($p<0.05$). The higher the numbers of live children lower the occurrences of gestational hypertension as depicted in table-4. There was

no significant association (p=0.377) between no. of abortions and gestational hypertension as shown in table-5.

There was no significant association between maternal blood group, child's sex and gestational hypertension (p values 0.496, 0.343 respectively) as seen in tables-6, 8. There was significant association between family history of cardiovascular disease and gestational hypertension ($p<0.001$) as in table-7. It was found that there was no significant association between the child's birth weight and gestational hypertension (p=0.077) as shown in table-9. There was a significant association between plasma homocysteine levels and gestational hypertension ($p<0.001$).

Positive correlation was found between plasma homocysteine levels and MAP(r=0.447, p=0.000), SBP(r=0.559, p=0.000), DBP(r=0.334, p=0.000). There was also positive relationship between family history and MAP, SBP, DBP(r=0.360, p=0.000, r=0.438, p=0.000, r=0.276, p=0.003 respectively) as depicted in table-11.

It was found in the study that there was no significant association between plasma homocysteine levels and age (p=0.851), parity (p=0.496) , no of live births (p=0.132), no of abortions (p=0.221),

child's sex($p=0.721$) and blood group($p=0.147$) as seen in tables-12,13,14,15,16&18. There was significant association between plasma homocysteine and positive family history of cardiovascular disease ($p<0.05$) as shown in table-17.

It was found that there was significant association between plasma homocysteine and birth weight of babies ($p<0.01$) as depicted in table-19. There was significant association between diagnosis and plasma homocysteine levels ($p<0.001$) as shown in table-10. It implies that homocysteine levels in preeclampsia are higher than that in gestational hypertension.

Ingec et al in 2005 showed that homocysteine concentration in severe preeclamptic and eclamptic women were significantly higher than mild preeclamptic and normotensive women concluding that elevated plasma homocysteine levels in early pregnancy can increase the risk of developing severe preeclampsia. These results are similar to our study.

Lopez et al in 2003 has results aligning with our study. It was concluded that plasma homocysteine levels in gestation hypertension and preeclampsia were higher than that in normotensive controls.

El abd et al in 2009 conducted a case control study similar to our study which stated that there was a positive correlation between plasma homocysteine levels and SBP, DBP and MAP. It was also found that no significant correlation existed between plasma homocysteine levels and women's age. It was found that MAP, SBP, DBP were higher in cases than in controls similar to our study.

Raijmaker et al in 2001 concluded in their study that plasma homocysteine levels were higher in preeclampsia and gestational hypertension compared to normotensives. This study is also similar to our study.

Amir et al in 2006 also conducted a case control study along the lines of our study and established that fasting plasma homocysteine levels were higher in cases than in controls.

Vincent et al in 2009 showed that mean homocysteine levels were higher in cases and a significant association existed between plasma homocysteine levels and gestational hypertension. It was also found that higher the homocysteine levels, higher are the SBP and DBP similar to our study.

In our study it has been established that a relationship exists between plasma homocysteine levels and gestational hypertension. Also it has been established that plasma homocysteine is higher if there is positive family history of cardiovascular disease. It was also found that plasma homocysteine levels are higher in preeclampsia than in gestational hypertension.

Summary

SUMMARY

A case control study comprising 111 participants with 50 cases and 61 controls was done. Cases were postnatal mothers with gestational hypertension with BP more than 140/90 mmHg. Controls were normotensive women comparable in all aspects. A fasting sample of plasma homocysteine was obtained from all the cases and controls. Plasma homocysteine was measured using the Chemi luminescence immunoassay method.

The data obtained was subjected to statistical analysis. It was found that the mean plasma homocysteine levels were higher in cases than in controls. It was also found that the plasma homocysteine levels were higher in preeclampsia than in gestational hypertension. If there was positive family history of cardiovascular disease then plasma homocysteine levels were found to be higher. Higher the SBP, DBP & MAP values, higher were the levels of plasma homocysteine. There was also evidence to state that there was association between elevated plasma homocysteine levels and birth weight of child.

Thus the study establishes the positive relationship between plasma homocysteine levels and gestational hypertension.

These results are in conjecture with several studies done already. The future implications of this study is that based on increased plasma homocysteine in women with gestational hypertension Homocysteine could a potential marker for predicting gestational hypertension.

Conclusion

CONCLUSION

It is concluded from this study that a relationship exists between plasma homocysteine levels and gestational hypertension. It is also concluded that higher levels of plasma homocysteine levels are found in women with gestational hypertension compared to normotensive pregnant women.

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Annexure

Proforma

TAMILNADU Dr M.G.R. MEDICAL UNIVERSITY

DEPT. OF OBSTETRICS AND GYNAECOLOGY

COIMBATORE MEDICAL COLLEGE

COIMBATORE

PROFORMA

Name :

Age & Sex :

IP. No. /Unit:

Parity:

Diagnosis:

Consent:

Case/Control:

Blood group:

Medical history:

Obstetric history:

Family history:

Admission BP:

Mode of Delivery:

Child-Sex/Weight:

Plasma homocysteine levels:

Master Chart

MASTER CHART

S.No	Name	Age	IPNo	Parity	Live	Abortion	Blood Group	Family H/O CVD	Diagnosis	SBP	DBP	MAP	Mode of Delivery	Sex of the child	Birth wt of Child	P.Homocysteine
1	Vanithamani	21	47899	1	1	0	B+ve	Positive	E	170	110	130	LN	2	2.6	22.5
2	Sivaranjini	20	47672	1	1	0	O+ve	Negative	E	172	110	130.67	LN	2	3.1	32.4
3	Gowri	24	41732	1	1	0	B+ve	Negative	PE	140	90	106.67	LSCS	2	3	11.28
4	Murugathal	21	46863	1	0	0	B+ve	Positive	E	180	90	120	LN	2	2.6	23.09
5	Arulmani	25	47888	1	1	0	A+ve	Positive	GHT	140	90	106.67	LSCS	1	2.4	7
6	Babu	33	48110	1	1	0	O+ve	Positive	GHT	140	90	106.67	LSCS	1	3.2	6
7	Kalamani	24	49202	2	1	0	O+ve	Positive	PE	160	90	113.33	LN	2	3	44.31
8	Masilamani	32	46370	3	3	0	A+ve	Positive	PE	140	90	106.67	LSCS	2	3	15.61
9	Neelavathy	28	48218	2	2	2	B+ve	Negative	PE	140	90	106.67	LSCS	2	2.8	24.62
10	Kumudha	22	47112	1	1	0	B+ve	Negative	PE	140	90	106.67	LSCS	1	2.7	19.34
11	Pandiselvi	27	49171	1	1	1	B+ve	Negative	PE	162	100	120.67	LSCS	2	2.6	15.56
12	Kalavathy	32	48142	2	2	0	B+ve	Negative	GHT	140	90	106.67	LSCS	1	2.4	11.36
13	Selvi	21	49642	1	1	1	A+ve	Negative	N	110	80	90	LN	2	3.2	13.04
14	Punitha	23	49514	1	1	0	B+ve	Negative	N	120	70	86.67	LN	1	3	15.15
15	Jameela	18	49607	1	1	0	A+ve	Negative	N	110	80	90	LN	2	3	11.45
16	Vennila	23	48976	3	3	0	O+ve	Negative	N	120	80	93.33	LN	1	2.8	16.92
17	Benazir banu	22	49720	2	1	1	A+ve	Negative	N	110	80	90	LN	2	2.7	9.97
18	Sneha	19	49990	1	1	1	B+ve	Positive	PE	160	100	120	LSCS	1	2.6	39.93
19	Pushpa	30	49822	3	3	0	A+ve	Positive	PE	140	90	106.67	LN	2	2.4	25.06
20	Baby	24	49862	1	1	0	A+ve	Positive	PE	160	110	126.67	LSCS	1	3.7	14.94
21	Lakshmi	27	50100	1	1	0	O+ve	Negative	PE	142	90	107.33	LSCS	2	3.1	14.26

22	Shanthi poorani	28	48058	2	1	1	B+ve	Negative	PE	160	100	120	LN	1	2.8	29.31
23	Rasmi	20	50012	1	1	0	O+ve	Negative	N	110	80	90	LN	1	3.7	16.08
24	Panchavarnam	25	49143	2	2	0	A+ve	Negative	E	170	110	130	LN	2	3	17.36
25	Vijayalakshmi	18	50303	1	1	0	B+ve	Negative	E	162	110	127.33	LN	1	3	24.95
26	Vijaya	23	50375	2	2	0	O+ve	Negative	PE	150	108	122	LSCS	1	2.8	16.89
27	Kalpana	21	50845	2	2	1	A-ve	Negative	N	110	70	83.33	LN	1	2.8	20.74
28	Geetha	23	49752	1	1	0	AB+ve	Negative	GHT	140	100	113.33	LSCS	1	2.6	13.65
29	Thilagavathy	22	49739	1	1	0	O+ve	Negative	GHT	140	100	113.33	LSCS	2	2.5	16.7
30	Krishnaveni	27	50605	2	3	0	B+ve	Negative	GHT	140	90	106.67	LN	2	3	27.85
31	Ranganayaki	24	50673	1	1	0	O+ve	Negative	PE	160	110	126.67	LSCS	1	2.8	19.07
32	Vijayalakshmi	24	51077	1	1	1	B+ve	Negative	PE	140	100	113.33	LSCS	1	2.8	12.1
33	Sarawathy	20	50709	1	1	0	O+ve	Positive	PE	150	90	110	LSCS	1	2.6	19.65
34	Amutha	24	50962	3	1	0	AB+ve	Positive	PE	160	90	113.33	LSCS	1	3	13.88
35	Jayanthi	26	51007	2	2	0	B+ve	Negative	GHT	140	100	113.33	LN	1	2.8	10.4
36	Rekha	22	51296	1	1	0	B+ve	Negative	GHT	140	90	106.67	LN	2	3	20.47
37	Kaliammal	21	51210	1	0	0	O+ve	Negative	GHT	140	90	106.67	LN	1	2.8	25.84
38	Sumathy	24	50533	3	3	0	A+ve	Negative	PE	160	110	126.67	LN	1	3	12.95
39	Thilaga	22	50546	1	3	0	B+ve	Negative	GHT	140	100	113.33	LN	1	2.8	28.82
40	Palaniyammal	27	51772	2	2	0	B+ve	Negative	PE	160	110	126.67	LN	1	2.4	53.83
41	Ruckmani	38	52888	4	4	0	A+ve	Positive	PE	150	90	176.67	LSCS	1	3	12.79
42	Benazer	18	52821	1	2	0	O+ve	Positive	PE	160	100	120	LN	2	3	19.88
43	Sakira Banu	22	52938	1	1	0	A+ve	Positive	E	180	110	133.33	LN	2	2.8	16.11
44	Sahana	18	53499	1	1	0	A+ve	Negative	PE	150	100	116.67	LSCS	1	3	20.01
45	Selvi	22	4467	2	2	0	B+ve	Negative	GHT	130	80	96.67	LN	1	2.6	9.12
46	Jothimani	21	9367	1	0	1	A+ve	Negative	GHT	140	100	113.33	LN	1	2.4	12.4
47	Rohini	21	9924	1	0	0	O+ve	Positive	GHT	140	100	113.33	LN	2	2.5	9.53
48	Kumudha	30	10772	2	2	0	O+ve	Negative	GHT	140	140	140	LN	2	2.8	16.08

49	Devaki	25	10128	1	0	0	O+ve	Positive	PE	150	100	116.67	LN	1	2.5	16.36
50	Gayathri	22	9272	1	1	0	A+ve	Positive	PE	150	100	116.67	LSCS	2	2.8	12.38
51	Mallika	22	9949	1	1	0	A+ve	Negative	E	160	112	128	LN	1	2.8	11.64
52	Abirami	20	10016	1	1	0	O+ve	Negative	PE	160	110	126.67	LSCS	1	2.6	19.11
53	Vasantha	20	9425	1	1	0	B+ve	Negative	PE	160	110	126.67	LSCS	1	2.9	6.89
54	Sumathi	23	9777	1	1	0	A+ve	Negative	PE	140	90	106.67	LSCS	1	3.4	16.06
55	Vasantha	27	10161	1	0	1	B+ve	Negative	E	160	110	126.67	LN	1	2.8	12.73
56	Jhansi	20	57136	1	1	0	O+ve	Negative	GHT	140	100	113.33	LN	1	3.1	29.84
57	Velumani	24	5399	1	1	0	B+ve	Negative	GHT	140	110	120	LN	2	2.9	17.75
58	Parveen banu	27	58377	1	1	0	A+ve	Negative	N	120	80	93.33	LN	1	3.7	14.78
59	Sivaranjani	21	66124	1	1	0	B+ve	Negative	N	120	80	93.33	LSCS	2	2.9	8.16
60	Suganya	22	66144	1	1	0	B+ve	Negative	N	120	80	93.33	LSCS	1	2.4	9.24
61	Saranya	19	66145	1	1	0	A+ve	Negative	N	120	80	93.33	LN	1	2.7	8
62	Naseema Begam	24	66167	1	1	0	O+ve	Negative	N	120	80	93.33	LN	2	2.7	6.22
63	Meharunnisha	20	65771	1	1	0	A+ve	Negative	N	120	80	93.33	LN	2	2.4	7
64	Seerangi	32	66176	1	1	0	A+ve	Negative	N	120	80	93.33	LSCS	2	2.9	10.2
65	Renuka	27	66186	2	2	0	B+ve	Negative	N	120	80	93.33	LN	2	2.8	11.44
66	Anupama	22	66205	2	2	0	B+ve	Negative	N	130	90	103.33	LN	2	2.8	12.34
67	Kavitha	20	66185	1	1	0	A+ve	Negative	N	120	80	93.33	LN	2	2.6	10.12
68	Shanthi	23	66236	2	2	0	O+ve	Negative	N	120	80	93.33	LN	1	3.25	11
69	Renuka	24	66217	2	2	0	A+ve	Positive	N	120	80	93.33	LSCS	2	3.2	9
70	Sarada	22	65892	1	1	0	A+ve	Negative	N	120	80	93.33	LSCS	1	2.9	7.88
71	Kanageswari	23	66235	1	1	0	B+ve	Negative	N	120	80	93.33	LSCS	1	3.2	8.78
72	Rani	20	66283	2	2	0	A+ve	Negative	N	120	80	93.33	LSCS	1	3.25	8
73	Deepa	23	66272	2	2	0	O+ve	Negative	N	120	80	93.33	LN	1	2.4	6.22
74	Arulmozhi	27	66292	1	1	0	O+ve	Negative	N	120	80	93.33	LN	1	3	7
75	Prema	23	66231	1	1	0	O+ve	Negative	N	130	90	103.33	LN	1	3	10.2

76	Vijayalakshmi	25	66296	1	1	0	A+ve	Negative	N	120	80	93.33	LN	2	2.5	11.12
77	Maheswari	25	66024	2	2	0	A+ve	Negative	N	120	80	93.33	LSCS	1	3.24	9.32
78	Kamatchi	25	66250	3	3	0	O+ve	Negative	N	120	80	93.33	LSCS	2	2.5	7.9
79	Kala	29	64817	2	2	0	B+ve	Negative	N	120	80	93.33	LN	2	1.4	8.56
80	Sasikala	26	64207	2	2	0	A+ve	Negative	N	120	80	93.33	LN	1	2.5	10.74
81	Radhika	20	66307	1	1	0	B+ve	Negative	N	120	80	93.33	LN	2	2.7	11.02
82	Shakunthalamani	26	66315	1	1	0	O+ve	Negative	N	120	80	93.33	LSCS	2	3.5	10.12
83	Latha	24	66149	2	2	0	O+ve	Negative	N	120	80	93.33	LN	1	2.5	15
84	Devika	30	66422	2	2	0	A+ve	Positive	N	120	80	93.33	LN	1	2.4	9.8
85	Vennila	21	66423	1	1	0	A+ve	Negative	N	120	80	93.33	LN	1	2.5	7.88
86	Sindhu	22	66450	2	2	0	B+ve	Negative	N	120	80	93.33	LN	1	2.7	8.78
87	Usha	21	66448	1	1	0	B+ve	Negative	N	120	80	93.33	LSCS	2	2.3	8
88	Santhi	23	66402	3	3	0	A+ve	Negative	N	120	80	93.33	LSCS	1	2.75	6.22
89	Nandhini	20	66074	1	1	0	O+ve	Negative	N	120	80	93.33	LN	1	2.4	8.16
90	Rajathi	20	66214	1	1	0	A+ve	Negative	N	120	80	93.33	LN	2	2.5	9.24
91	Poongodi	23	66538	2	2	0	A+ve	Negative	N	120	80	93.33	LN	2	2.5	13.8
92	Jayasudha	28	66063	2	2	0	B+ve	Negative	N	120	90	100	LN	1	3.6	6.26
93	Mariammal	24	65150	2	2	0	A+ve	Negative	N	120	80	93.33	LSCS	1	2.5	14.12
94	Sathyakala	24	64182	2	2	0	O+ve	Negative	N	120	80	93.33	LSCS	1	2.7	10.2
95	Sudha	24	66536	2	2	0	O+ve	Negative	N	120	80	93.33	LN	1	2.5	9.32
96	Anitha	21	66542	1	1	0	O+ve	Negative	N	120	80	93.33	LN	2	3.1	7.9
97	Busra	28	66647	4	4	0	A+ve	Negative	N	120	80	93.33	LSCS	2	3.1	8.56
98	Sakeelabanu	20	65742	1	1	0	A+ve	Negative	N	120	80	93.33	LSCS	1	2.9	12.32
99	Nimmy	29	66693	2	2	0	O+ve	Negative	N	120	80	93.33	LSCS	1	2.75	13.62
100	Rajeswari	22	66707	1	1	0	B+ve	Negative	N	120	80	93.33	LN	1	2.75	10.2
101	Jhansi	20	66736	1	1	0	A+ve	Negative	N	120	80	93.33	LN	2	2.5	11.12
102	Sapna	21	66684	2	2	0	B+ve	Positive	N	130	80	96.67	LN	2	2.7	9.32

103	Jayanthi	20	66577	1	1	0	O+ve	Negative	N	120	80	93.33	LN	2	2	7.9
104	Saini	23	66702	1	1	0	B+ve	Negative	N	120	80	93.33	LSCS	2	2.9	8.56
105	Gayathri	21	66743	2	2	0	A+ve	Negative	N	120	80	93.33	LSCS	1	3	10.74
106	Soniadevi	22	66783	1	1	0	O+ve	Negative	N	120	80	93.33	LN	1	2.75	11.02
107	Pushpanjali	24	66599	2	2	0	A+ve	Negative	N	120	80	93.33	LN	1	3.25	10.12
108	Dhanalakshmi	23	66576	1	1	0	O+ve	Negative	N	120	80	93.33	LN	2	3.5	14.24
109	Santhi	27	66846	2	2	0	B+ve	Negative	N	120	80	93.33	LSCS	2	3	12
110	Selvi	20	66727	2	2	0	O+ve	Negative	N	120	80	93.33	LN	1	2.5	13.55
111	Gandhimathi	28	66543	1	1	0	B+ve	Negative	N	120	80	93.33	LN	2	2.7	14.68

Note:Age in years, N- Normal,GHT-Gestational hypertension,PE-Preeclampsia,E-Eclampsia,Family H/O CVD-Family History Of Cardiovascular Disease,In Sex of child 1- Male & 2- Female,P.Homocysteine in µmol\L, LN-Labour Naturale,LSCS-Lower segment caesarean section , Weight (Wt) in Kg & SBP,DBP,MAP in mmHg.

Abbreviations

ABBREVIATIONS

1	**BP**	**Blood pressure**
2	**PIH**	**Pregnancy induced hypertension**
3	**ALT**	**Alanine aminotransferase**
4	**AST**	**Aspartate aminotransferase**
5	**LDH**	**Lactate dehydrogenase**
6	**WKS**	**Weeks**
7	**PGI_2**	**Prostacyclin I_2**
8	**TXA_2**	**Thromboxane A_2**
9	**NO**	**Nitric oxide**
10	**NK cells**	**Natural killer cells**
11	**GFR**	**Glomerular filtration rate**
12	**VEGF**	**Vascular endothelial growth factor**
13	**PLGF**	**platelet growth factor**
14	**CTB**	**Cytotrophoblast**
15	**STB**	**Syncytiotrophoblast**
16	**Flt-1**	**Fms like tyrosine kinase-1**

17	**KDR**	**Kinase insert domain containing receptor**
18	**S.Flt-1**	**Soluble Fms like tyrosine kinase-1**
19	**S.ENG**	**Soluble endoglin**
20	**HLA**	**Human leukocyte antigen**
21	**KIR**	**Killer cell immunoglobulin like receptors**
22	**TGF-b**	**Transforming growth factor –b**
23	**TNF**	**Tumor necrosis factor**
24	**IFN**	**Interferon**
25	**THF**	**Tetrahydrofolate**
26	**SAM**	**S adenosyl methionine**
27	**MTHFR**	**Methylene tetrahydrofolate reductase**
28	**CBS**	**Cystathionine beta synthase**
29	**MS**	**Methionine synthase**
30	**HRT**	**Hormone replacement therapy**
31	**OCP**	**Oral contraceptive pills**
32	**LDL**	**low density lipoprotein**
33	**LP(a)**	**Lipoprotein(a)**
34	**Apo**	**Apo lipoprotein**

35	**DVT**	**Deep vein thrombosis**
36	**IUGR**	**Intrauterine growth restriction.**
37	**EDTA**	**Ethylene diamine tetra acetic acid**
38	**MAP**	**Mean arterial pressure**
39	**SBP**	**Systolic Blood Pressure**
40	**DBP**	**Diastolic Blood Pressure**